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ORIGINAL ARTICLES

**OPEN-AIR TREATMENT OF PNEUMONIA AND ANEMIA IN  
CHILDREN.<sup>1</sup>**

BY ROWLAND G. FREEMAN, M.D.,

NEW YORK.

THE importance of fresh air in the treatment of certain diseases is now well established. The best results from fresh-air treatment are obtained when the air is cold, when it is freely moving in an open space, and when the individual is kept in it twenty-four hours a day.

Little children tolerate poorly the stagnant air of most American houses in winter, and while inappropriate food is perhaps the most important cause of sickness in children, housing in winter is a close second. Severe cases of rachitis develop only in winter and in climates where babies are kept housed, and they develop under these conditions no matter what the food; and children of an ancestry from tropical climates suffer more from the housing than others, notably negroes and Italians.

Between the close, stagnant, indoor air that induces rachitis and pneumonia and the free-flowing, outdoor air there are many gradations due to methods of ventilation. The scientific forced ventilation which is interfered with by the opening of windows is expensive, occupies much space, and is usually inefficient. Open windows give a freshness to the air of a room that is never attained by scientific forced ventilation. The fear of a draught has been

<sup>1</sup> Read before the Association of American Physicians, Washington, D. C., May 12, 1915.

deeply impressed on all the last generation and many of the present. Too much access of air for comfort is best avoided by cheese-cloth screens. These were used many years ago by Henry Hun in the Albany Children's Hospital, and are today more satisfactory, I believe, than the patent ventilators made to place under an elevated window sash. In Dr. Hun's Hospital each window had two sets of sash, one pair carrying glass and the other cheese-cloth. The windows were usually kept open, the air entering freely through the cheese-cloth sash. These wards were always fresh and free from hospital odors, and the children in this institution did wonderfully well. While this method gives one perhaps the best indoor air for those requiring warm, still air, one may obtain far better results in the cold, fresh, outdoor air in winter.

It has long been an accepted fact among certain specialists in diseases of children that exposure to fresh, cold, moving air stimulates the circulation, puts color in the cheeks, increases the vigor of the body, the appetite, and the assimilation of food. While this has been applied particularly to children sick with a limited range of illness, especially pneumonia and tuberculosis, equally good results are derived from the use of this outdoor fresh-air treatment in bronchitis, anemia, chorea, marasmus, and measles as well as in all children lacking in vigor but with no tangible disease.

An excellent explanation of the action of this fresh air on the body functions was made by Howland and Hoobler, who published the results of a series of experiments on children with pneumonia and tuberculosis at Bellevue Hospital, when they reported that they found a marked increase in blood-pressure from putting the children outdoors and an equal diminution in blood-pressure when the children were returned to the closed wards of the hospital. This seemed so rational an explanation that it was generally accepted and hardly seemed to need confirmation, but although several years have elapsed, no confirmation of these results has been published so far as I know.

In work done under the writer's supervision at the New York Foundling Hospital and at the New York Nursery and Child's Hospital by Dr. Schloss no corroboration of these results could be obtained, while at The Roosevelt Hospital, Dr. Hartshorn has carried out a considerable series of blood-pressure experiments, with no constant results. We are thus unable to confirm the results of Howland and Hoobler.

While some children have shown a considerable increase in blood-pressure on being put outdoors, others have shown no increase, while on the other hand, there has been no constant fall of blood-pressure noted in returning the children to the ward. In fact, we find that the blood-pressure, on the average, is no higher outdoors than in the ward.



Pneumonia of infancy is a disease of housing. It has little tendency to develop in summer and is rarely found in winter in children that are kept in the open air. While for the cure of the disease an agent that is more efficient than any drug or serum or vaccine that is available at present is the freely moving outdoor air, and bronchitis and croup are no contra-indication to the use of this method of cure. A laboratory worker, Dr. A. W. Williams, after reviewing the various methods of treating pneumonia in the *Monthly Bulletin* of the New York City Board of Health, closes her article as follows: "Hygienic treatment, in which absolute rest and free exposure to the outdoor air is the main reliance, seems of late years to have greatly reduced the death-rate, and, until specific therapy is upon a sure footing, will remain the method of choice with most clinicians."

I have been able to carry on some interesting experiments in fresh-air treatment in The Roosevelt Hospital.

The Medical Pediatric Division of The Roosevelt Hospital consists now of a ward of eight beds, a quarantine ward of four beds, and a roof, partly covered by a shed and enclosed on the north, east, and west sides, with seven beds. They all are on the same floor and adjacent to each other, an arrangement that lends itself well to fresh-air treatment.

The bedsteads are painted with white enamel, which is not injured by dampness or wet, and are thus well adapted for this purpose. Ample bedclothes are provided for use in cold weather, as well as sufficient appliances, such as hot-water bags or heaters to keep the extremities warm. Mitts may be needed on the hands, while in very cold weather a cap for the head is desirable. The children are kept on the roof, not for a few hours each fine day, but day and night during all weather. Care is taken, particularly by feeling the feet, to see that the children are comfortably warm; they are brought into the wards only to be changed, bathed, or dressed.

An advantage of such outdoor treatment is the marked lessening of communicability. We have had cases of measles develop on our roof which were followed by no subsequent cases evidently due to these cases. This is an experience rarely met with in hospital wards.

Ten years ago a good deal was written concerning this outdoor treatment of hospital cases, particularly by Dr. Northrup, and while the results obtained continued satisfactory, this method of treatment has gradually fallen into disuse. Moreover, the application of this treatment has usually not been very thorough. A child would be kept outdoors a certain number of hours each day, but rarely have they been kept outdoors all the time.

The conditions which have seemed in our service to be most benefited by this fresh-air treatment are pneumonia, tuberculosis,

anemia, chorea, marasmus, and convalescents from any disease. Kidney and heart cases we have thought best to keep in the wards, although one child that had nearly died with endocarditis and pericarditis seemed during convalescence to have been much improved by living on the roof in winter, and this was allowed at his request, and was apparently much enjoyed by him.

I wish particularly to emphasize the fact that our wards are kept cool and well ventilated, so that any comparison between the ward and the roof is a comparison between a fairly open ward and a roof-shed.

The one disease that is most generally accepted as benefited by fresh-air treatment is pneumonia.

The method of treating these cases in The Roosevelt Hospital has been to give them an initial dose of castor oil, put them in beds on the roof, keep their extremities warm and their bowels open. Very few of the cases have received any stimulant or expectorant. In some cases when the cough was troublesome a dilute solution of tincture of chloride of iron in glycerin or water has been used.

Before considering our results of treatment of these pneumonias it will be of advantage to arrive at some idea of the mortality of pneumonia in children. Osler states that the mortality from bronchopneumonia in children is 50 per cent. Holt gives a mortality of 5 per cent. for lobar pneumonia, but from bronchopneumonia in private practice from 10 to 20 per cent.; in uncomplicated bronchopneumonia in institution children of 50 per cent. and in complicated pneumonia of from 80 to 100 per cent., while classifying them by age he gives as the mortality of 346 cases during the first year, 66 per cent.; second year, 55 per cent.; third year, 33 per cent.; fourth year, 16 per cent. The mortality of the last 42 cases of lobar pneumonia at the New York Nursery and Child's Hospital, where conditions are very good, was 19 per cent., while that of the last 221 cases of bronchopneumonia was 33 per cent. In the New York Foundling Hospital, where the children are mostly under three years of age, the last 114 cases of lobar pneumonia showed a mortality of 32 per cent., while the last 736 cases of bronchopneumonia gave a mortality of 51 per cent. Of the last 108 cases of pneumonia treated at the Pediatric Service at The Roosevelt Hospital 21 were discharged as improved or unimproved, leaving 87 that remained to the termination of the disease. Of these 87 cases 25 were lobar pneumonia and 62 were bronchopneumonia. Of the 25 cases of lobar pneumonia three died, giving a mortality of 12 per cent., while of the 62 cases of bronchopneumonia 16 died, giving a mortality of 26 per cent.

Many of these cases were complicated: one turned out at autopsy to be tuberculosis, and in others death really was precipitated by other diseases. Perhaps the best estimate of our results is obtained by considering our uncomplicated cases of pneumonia: The 21

cases of uncomplicated lobar pneumonia showed one death in a child of six months, giving a mortality of 4.7 per cent., while the 31 cases of uncomplicated bronchopneumonia showed only one death in a child of nine months, giving a mortality of 3.3 per cent.

These uncomplicated cases of bronchopneumonia ran an average course after admission of seven days, and the cases of uncomplicated lobar pneumonia ran an average course after admission of three days.

One case of particular interest was that of a colored boy, aged five years, who came into the hospital with typhoid fever. He ran the ordinary four weeks' fever, followed by a relapse of two weeks, at the end of which time, after having been in the ward eight weeks, he developed pneumonia and was immediately put on the roof. The pneumonia involved first the right upper lobe, then the left lower and the right middle lobe. The breathing was bronchial on the right side, and soon we found developing on our Röntgen-ray plates two cavities in the right middle lobe. These became larger, the sputum became foul, and physical signs of these cavities developed. The boy was desperately sick for a long time, but was finally discharged eighteen weeks after admission, with a practically normal temperature. He has since made a good recovery and has been at school during the past winter. This boy would, I believe, have certainly died if he had not been put on the roof.

Recently he has been returned to our ward with signs of consolidation over the right middle lobe, with a Roentgen-ray plate that shows the presence of the old cavities with consolidation in the neighborhood, and areas that are fairly typical of tuberculosis. He was running a moderate temperature, with marked remissions, and was vomiting on admission. During the days he has been on the roof his temperature has become more moderate, he has stopped vomiting, his appetite has improved, and his last roentgenogram shows a marked clearing of the areas of consolidation in his lungs.

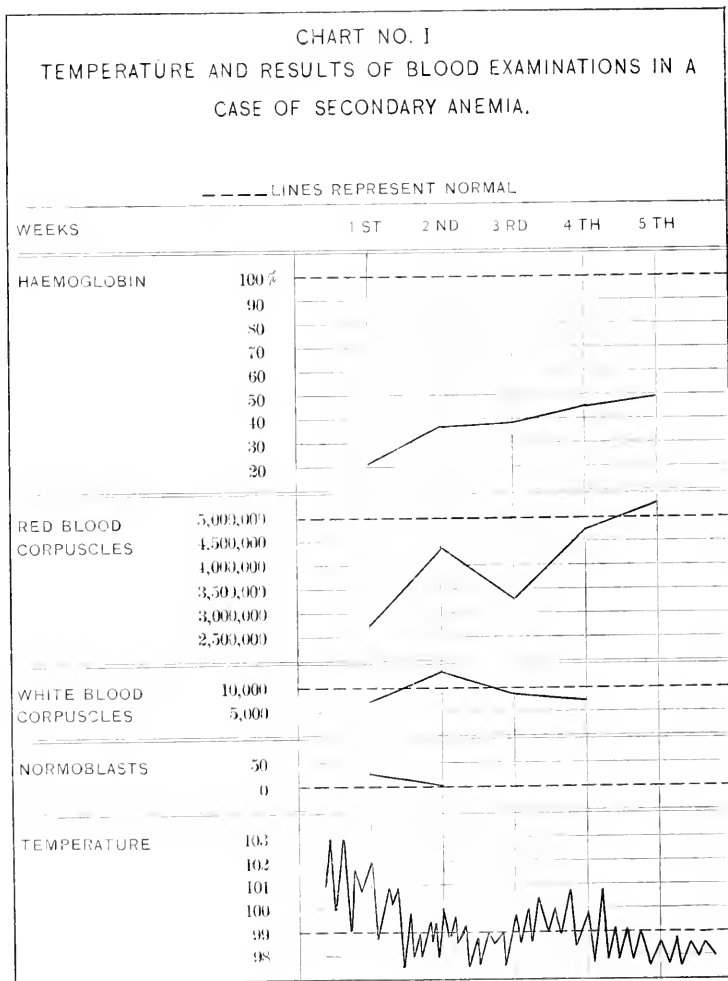
Perhaps our most interesting results of the roof treatment have been in the cases of abnormal conditions of the blood. One simple anemia made a wonderfully speedy recovery, with little medicine and roof treatment.

A poorly nourished child, aged thirteen months, came to our service running a considerable temperature of from  $101^{\circ}$  to  $103^{\circ}$ , with bronchitis, gastro-enteritis, and a marked simple anemia. The hemoglobin was only 22 per cent.; red cells, 2,840,000; white cells, 7700. There was moderate poikilocytosis and anisocytosis (Chart I).

This child was given seven drops of syrup of iodide of iron three times daily in addition to the treatment on the roof. The improvement was very rapid, the temperature in a week having reached normal, while in four weeks from admission the hemoglobin was 45 per cent., and the red cells 5,030,000. The weight had increased

one pound. The respirations had fallen from 38 to 29. The pulse had dropped from 136 to 100. The rapid improvement of this child is well shown on Chart I.

A very marked case of von Jaksch's anemia occurred in a colored child, a Porto Rican, aged three years. The child complained



of fever and headache, had a large spleen, and ran a temperature of 102° for ten days after admission. She was put on the roof and was given no medicine excepting such as might have been necessary to keep her bowels open. Her blood count on admission was: Hemoglobin, 17.5 per cent.; red blood cells, 1,368,000; index,

0.77; white blood cells, 41,000; polynuclears, 74 per cent.; lymphocytes, 26 per cent.; megaloblasts, 10; anisocytosis and poikilocytosis. The blood count showed a markedly typical von Jaksch's anemia condition.

Eight days later the blood had improved, as shown on Chart II. The next week showed still further improvement, the normoblasts and megaloblasts having nearly disappeared, while on April 29 the child was so well that she was discharged, the spleen, however, remaining large.

Six weeks later the child returned with pneumonia, the blood, however, being much the same as when the child was discharged, showing none of the changes characteristic of von Jaksch's anemia. The child made a recovery on the roof from pneumonia and was not seen again until last January, when she came in with the following blood count: Hemoglobin, 25 per cent.; red blood cells, 1,600,000; index, 1.1; white blood cells, 50,000; polynuclears, 70 per cent.; lymphocytes, 27 per cent.; myelocytes, 3 per cent.; normoblasts, 48; megaloblasts, 18. Anisocytosis and poikilocytosis. Red blood cells: largest, 12.6 m.; smallest, 2.1 m.

The spleen remained about the same size. Normoblasts and megaloblasts were present in considerable numbers, and there was a considerable increase in the number of white cells and a diminution in the red cells.

One week on the roof almost eliminated the normoblasts and megaloblasts and brought the white cells down to normal. At that time it occurred to me that the improvement in the child's condition might not be due to the roof treatment but might be due simply to hospital care. Therefore on January 20 the child was put in the ward. The temperature immediately began to rise, and although we had contemplated leaving the baby in the ward for a week, on the sixth day the child was doing so badly it was felt that it was not fair to leave her there any longer, and she was taken to the balcony. At that time the blood had changed as follows: Hemoglobin, 33 per cent.; red blood cells, 1,600,000; index, 1.2; white blood cells, 17,400; polynuclears, 60 per cent.; lymphocytes, 32 per cent.; myelocytes, 8 per cent.; megaloblasts, 4.

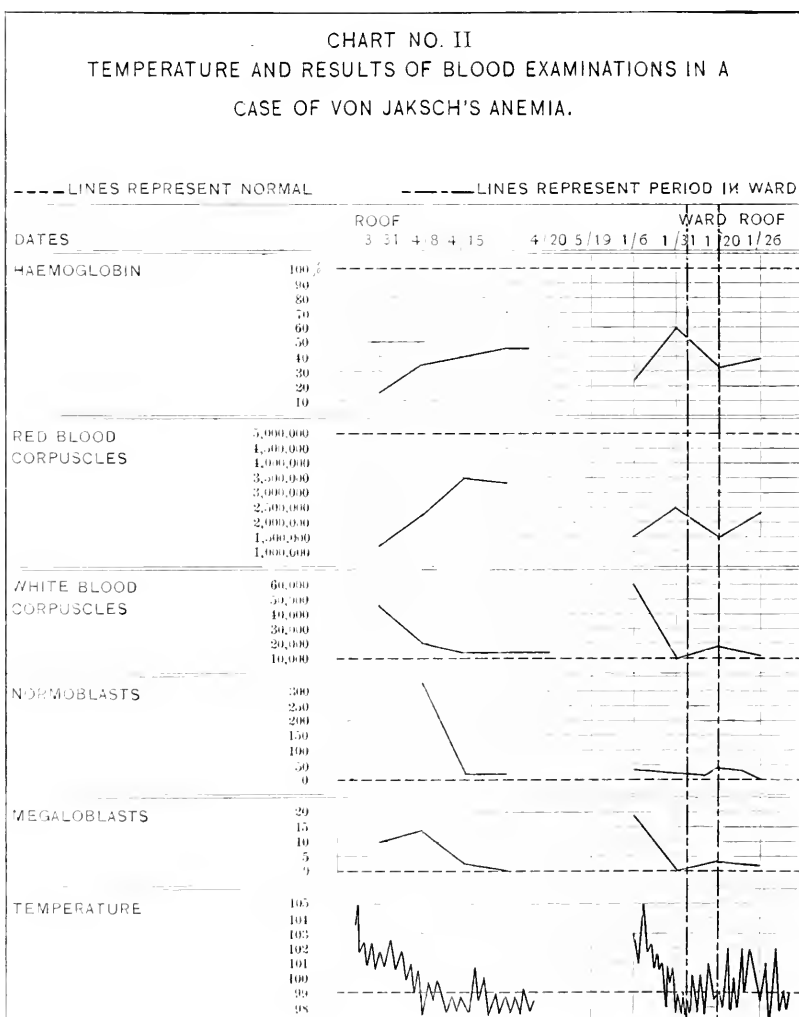
After a week on the balcony there was a marked improvement in the blood count, as indicated below: Hemoglobin, 36 per cent.; red blood cells, 2,400,000; index, 0.9; white blood cells, 14,400; polynuclears, 56 per cent.; lymphocytes, 35 per cent.; myelocytes, 0; normoblasts, 2; megaloblasts, 1.

During this time the child's temperature returned to normal, but, unfortunately, she showed gonococci in a vaginal smear and had to be transferred.

Chart II shows well the approach to normal of the abnormal condition of the blood as well as the lowering of the temperature while on the roof; the return toward the original condition on

admission during the six days in the ward, and the subsequent improvement on the roof.

A third child, aged four years, of French and German parentage, a case of leukemia, gave a history of cough for four months, swelling



of the neck for four weeks, dyspnea, constipation, pains in legs and arms, anorexia, and fever for a few days. He had dysentery when six months old. His complexion had always been yellow.

Physical examination showed a fairly well-developed boy, with skin so dark as to suggest mulatto blood. He was evidently

anemic and looked sick. There was slight dyspnea, with inspiratory stridor and slight cough. The tongue was moist and clear. The teeth were decayed. There was a general enlargement of the lymph glands all over the body. The parotid and submaxillary glands were markedly enlarged but not tender, while large masses of lymph nodes filled up the neck. Large groups of lymph nodes were in both axillæ, extending out over the anterior chest wall. The epitrochlears were felt, and the inguinal glands were markedly enlarged. The chest showed a diminished excursion on the left



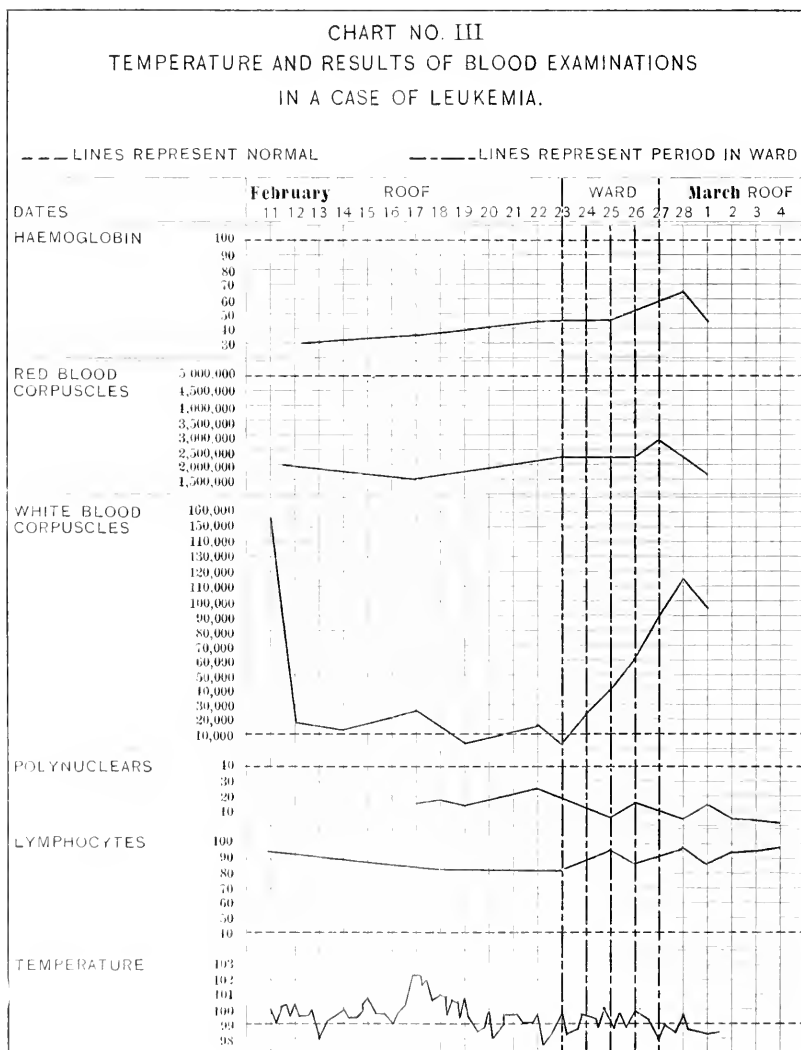
FIG. 1.—The child with leukemia, showing lymph-node enlargement indicating the lower border of the liver as well as the outline of the spleen.

side. There was on the same side some dulness, with, however, a rather tympanitic note over the scapula. There were a few moist rales on this side, with diminished breathing of a somewhat bronchial type. The abdomen was large, showing a markedly enlarged liver and spleen, as indicated in the sketch (Fig. 1), the spleen extending seven and one-half inches below the free border of the ribs in the mammary line and one and one-quarter inches to the right of the midline at the navel.

The blood count showed: hemoglobin, 30 per cent.; red blood



cells, 2,000,000; white blood cells, 158,400; neutrophils, 2 per cent.; basophils, 1 per cent.; small lymphocytes, 5 per cent.; large lymphocytes, 90 per cent.; toxic irritation, 2 per cent.; anisocytosis and poikilocytosis.



The Roentgen-ray plate showed a consolidation of practically all of the left lung, while an exploratory puncture of the left chest withdrew a few drops of turbid amber fluid.

This child was placed on the roof where, as may be seen by Chart III, the white cells dropped in twenty-four hours from 158,400 to 15,000. The general appearance improved and the child began to get color in his cheeks. Each Roengten-ray plate showed further

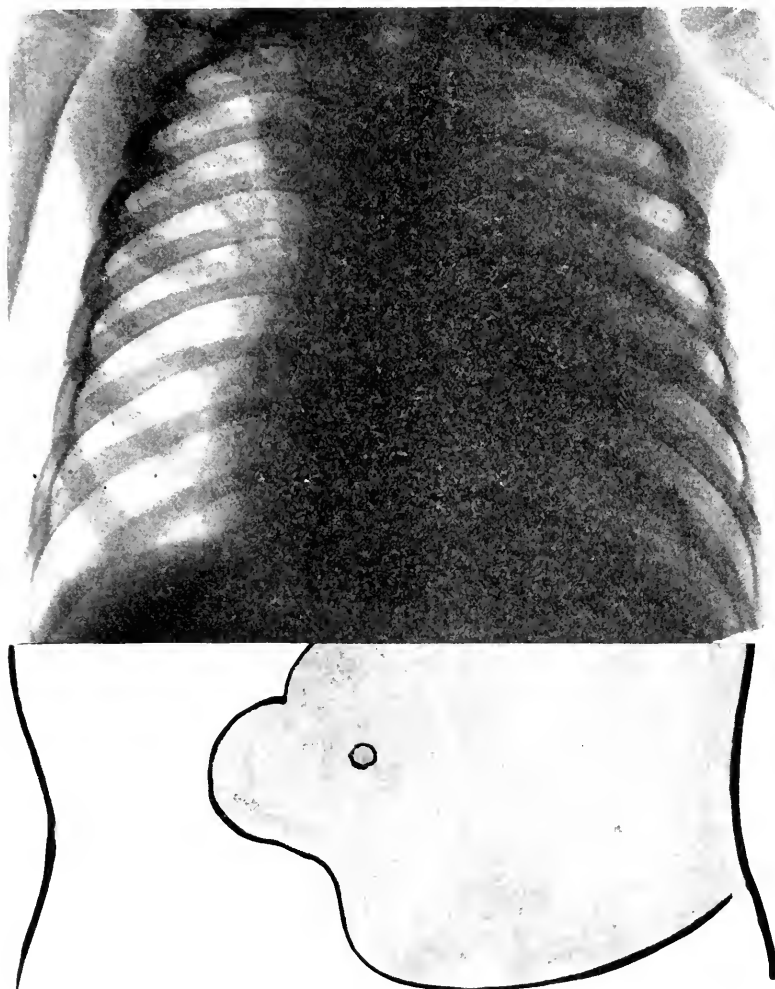


FIG. 2.—Leukemia case on admission, showing size of spleen and shadow in left lung.

clearing up of the pneumonia and physical examination showed a diminution in the size of the spleen, so that on the thirteenth day after admission all the lymph nodes as well as the salivary glands having diminished in size, the spleen having contracted from seven and one-half to four and one-half inches below the free border of the

ribs and no longer coming forward to the median line, a considerable portion of pneumonia having cleared up, as shown by the Roentgen-rays, and the blood having a normal number of leukocytes and being improved in other respects, the child was put in the ward. In this ward during a considerable part of the time that the child was in

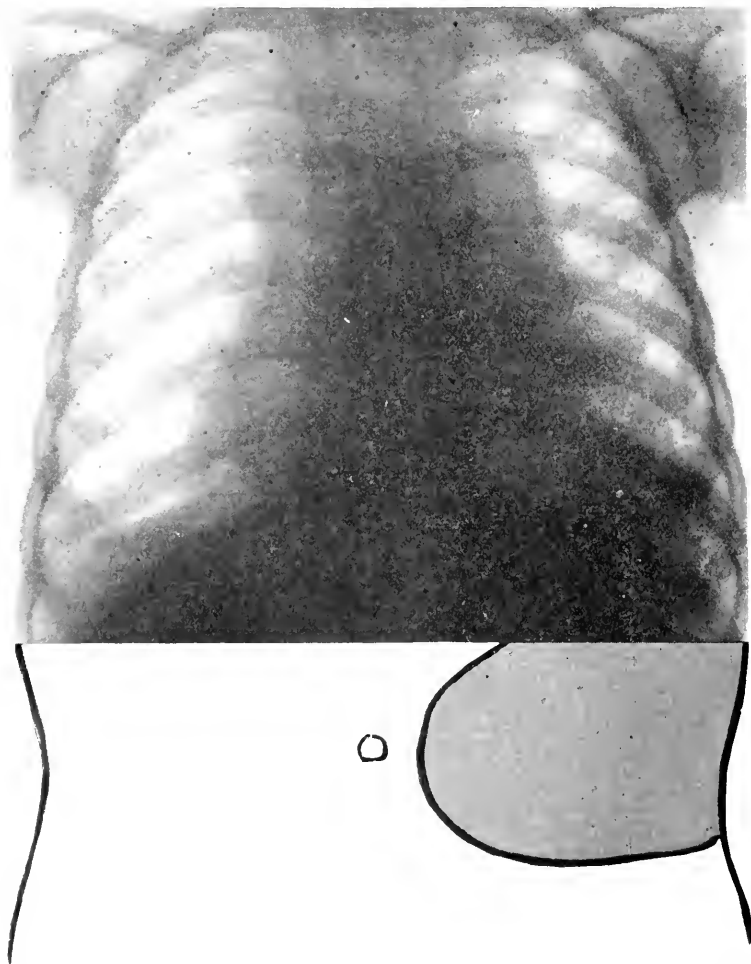


FIG. 3.—Leukemia case after twelve days on the roof, showing diminution in shadow made by left lung and diminution in size of spleen.

it, the windows at both ends were open and it was always well ventilated.

At the end of four days in the ward the lymph nodes were as large as they were on admission. The spleen had again extended beyond the median line, and to seven and one-half inches below

the free border of the ribs. The leukocytes, which had been daily increasing, had reached again 90,000, so that it seemed unfair to keep the child longer under these conditions, and he was again removed to the roof. Fig. 3 shows well the diminution in the shadow made by the left lung and the diminution in size of the

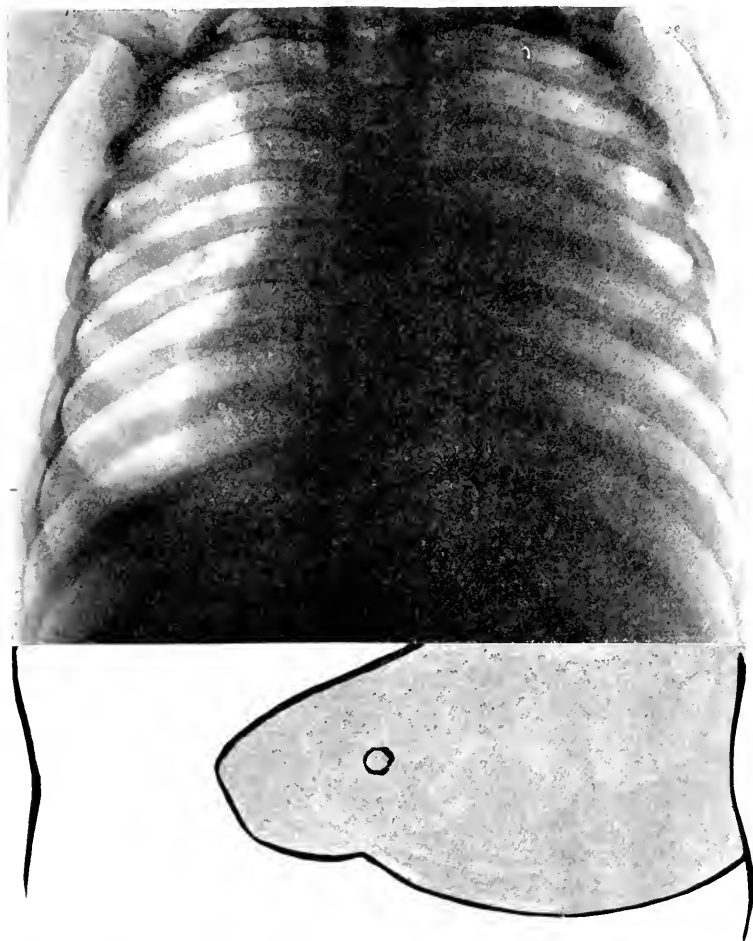


FIG. 4.—Disastrous effect on leukemia case of only four days in a well-ventilated ward.

spleen after the patient had been on the roof twelve days, while Fig. 4 shows the disastrous effect of only four days in a well-ventilated ward.

It is, of course, evident that three cases of sickness associated with abnormal conditions of the blood are not sufficient for drawing any conclusions, but in at least two of these cases it does seem as

if a fairly reliable demonstration of the influence of fresh air alone had been made.

SUMMARY. Treatment of children in an open-air shed in winter increases their vitality and resistance to disease more powerfully than medicines.

Pneumonias run a short course and show a very low mortality. Certain abnormal conditions of the blood will rapidly improve with little or no medical treatment.

## A PRELIMINARY REPORT ON PNEUMONIA IN CHILDREN, WITH SPECIAL REFERENCE TO ITS EPIDEMIOLOGY.<sup>1</sup>

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THE importance of pneumonia as a cause of death is hardly to be exaggerated. According to the United States census of 1900, pneumonia accounts for 3 per cent. of all diseases, with a mortality rate of 6.6 per cent., or of 12.7 per cent. if only medical cases are considered. It averages not less than 1.5 to 2.3 deaths per 1000 persons living. If pneumonia may be called the "old man's friend," it is just as certainly the enemy of youth, and especially of infancy. During early life the most common seat of organic disease is the lung, and some form of pneumonia is a large—perhaps the largest—factor at the present time in infant mortality. It is perhaps the only infectious disease in which the etiological cause supposedly is well understood whose incidence and rate have not been affected by such knowledge.

It is a matter of reproach to the profession that one hundred years of progress and varied methods of prevention and treatment have not affected the mortality rate of pneumonia in either adults or children.

The importance of pneumonia as a disease of infancy is well illustrated from the following mortality table of 1000 cases, which covers a period of the last nine years in the Babies' Wards of the New York Post-Graduate Hospital. The children were all under six years of age.

<sup>1</sup> Read at the Annual Meeting of the American Pediatric Society, May, 1915.

TABLE I.—1000 CASES OF PNEUMONIA FROM THE BABIES' WARDS OF THE NEW YORK POST-GRADUATE HOSPITAL.

		Per cent.
Cured	513	51.3
Dead	313	31.3
Improved	62	6.2
Unimproved	15	1.5
Termination not known	4	0.4
Transferred	63	6.3
Total	1000	100.0

That this mortality rate is not excessive is shown by a death rate of 33.1 per cent. obtained from a series of 410 cases collected by Holt.<sup>2</sup> Holt's series included 223 cases of bronchopneumonia and 187 cases of lobar pneumonia in children. The age incident is apparently about the same in the two series. Pneumonias secondary to infectious diseases, such as whooping cough, measles, etc., are not included in either group of cases.

Pfaundler has made the observation that children are ill of nutritional disturbances, but that they die of infection. The truth of that statement is supported by 84 of our cases of pneumonia, which were frankly secondary to other disturbances, with a mortality rate of 52 per cent. Of these 84 cases, 24 occurred as a complication of malnutrition, rickets, and enteritis, with a death rate of 62.5 per cent.

From the clinical stand-point, pneumonia seems naturally to fall into two groups, namely, (1) bronchopneumonia, and (2) lobar pneumonia. The differentiation between the two types is important from the stand-point of prognosis, of treatment, and of prevention, and undoubtedly could and should be made more frequently. It is proposed tentatively to prove that the two conditions of bronchopneumonia and lobar pneumonia are not identical either pathologically or bacteriologically.

Bronchopneumonia undoubtedly occurs as a primary condition, but most frequently is secondary to other diseases, such as bronchitis or a moderate or severe intestinal disturbance. A large percentage of the cases in children occur during the first two years of life, though it may occasionally be met with at any age. Of 445 cases treated in the Babies' Wards of the Post-Graduate Hospital during the first three years of life, 41 per cent. died. In the following table it will be noted that the number of cases of bronchopneumonia rapidly diminishes after the second year, so that in this series of 1000 cases, of which 445 were bronchopneumonia, there are only 31 cases of bronchopneumonia between the ages of four and six years. In other words, of 445 cases of bronchopneumonia, 414 were infections of the first three years of life, and more than half of all the cases in this group occurred during the first year.

<sup>2</sup> Diseases of Infancy and Childhood, 6th ed., pp. 515-535.

TABLE II.

	Post-graduate cases.		Holt's cases.	
	Cases.	Mortality, per cent.	Cases.	Mortality, per cent.
During the 1st year . . . . .	226	52.2	202	66.0
" 2d year . . . . .	155	29.0	102	55.0
" 3d year . . . . .	33	24.2	33	33.0
" 4th year . . . . .	13	0.0	6	16.0
" 5th year . . . . .	13	0.0	3	0.0
" 6th year . . . . .	5	0.0		

Of the lobar pneumonia cases there were 227, and they are fairly evenly distributed throughout the first six years, though the first and second years include more than half the total number. It will be noted that the mortality rate is distinctly lower than for bronchopneumonia, being for the entire six years 28.1 per cent. If the first two years of high mortality are eliminated the death rate falls to 10.8 per cent.

In the following table is seen the incident of mortality by age in 227 cases of lobar pneumonia studied:

TABLE III.—LOBAR PNEUMONIA.

	Cases.	Mortality, per cent.
During 1st year . . . . .	75	40.2
" 2d year . . . . .	97	34.0
" 3d year . . . . .	31	12.9
" 4th year . . . . .	25	16.0
" 5th year . . . . .	21	0.0
" 6th year . . . . .	14	0.7

Judging from this series of 1000 cases of pneumonia, empyema is not a frequent complication. In all there were 41 cases, or 4.1 per cent., of empyema, of which 5 followed bronchopneumonia, the other occurring as a complication of lobar pneumonia.

Pathologically, it is questionable whether empyema ever occurs in a true case of bronchopneumonia. Wollstein and Meltzer,<sup>3</sup> in experimental bronchopneumonia on dogs, by means of intrabronchial insufflation, found practically complete absence of pleurisy in 20 experiments, while in true lobar pneumonia there was always a definite pleurisy even in non-fatal cases. Consequently, there must be some questioning of the 5 cases in this series which appear as a complication of bronchopneumonia. A few cases of empyema due to streptococcus have been reported, but the only case which has come directly under our observation was one of *Streptococcus hemolyticus*, occurring as a complication of an undoubted lobar pneumonia due to the pneumococcus.

It should be added that these 41 cases include only those empyemas which occurred as a complication of a pneumonia treated in the wards, and consequently have no relation to the total number of empyemas admitted to the hospital.

<sup>3</sup> Jour. Exper. Med., 1912, xvi, 126.



In a study of groups of pneumonia by months it may be easily shown that the mortality rate at certain times is unusually high, as, for instance, during January and February of 1915. The large number of cases which were fatally ill during these months, which was much higher than for corresponding months of other years—in fact, was the inspiration for the special bacteriological study—the results of which are detailed in this paper.

The most obvious explanation for the variation of the mortality rate of pneumonia from year to year and from month to month is found in a difference in the virulence of the pneumococcus, a highly virulent organism resulting in many deaths and extraordinary severe pneumonias; an organism of low virulence, on the other hand, giving an infection in which recovery is the more common outcome.

Opposed to the argument that pneumonia arises when organisms of increased virulence reach the lung is the fact that pneumonia rarely occurs in epidemics. A few such epidemics, however, have been described, the most widely advertised of which occurred in Panama during the first year of the American occupation, and the one in South Africa, which reached such proportions as to seriously menace the working of the mines. Curschmann<sup>4</sup> describes an epidemic which was supposed to be due to influenza, in which cultures showed, in 49 cases, pneumococci in almost pure culture. The organisms were highly virulent for mice, and presented other characteristics of pneumococci. Leeds<sup>5</sup> describes another such epidemic in which a most careful search for the influenza bacillus was completely negative and the infecting organism was unquestionably the pneumococcus. A careful scrutiny of our cases fails to reveal any evidence of an epidemic or even of a house infection. In 50 cases very carefully studied from all stand-points there is only 1 case in which the pneumococcus was apparently transmitted from a twin sister, and in this instance the type was that of a broncho-pneumonia.

Cole,<sup>6</sup> following the method of Lamar and Meltzer, of bronchial insufflation with broth cultures of various strains of pneumococci, has been able to prove that in rabbits, at least, the production of lobar pneumonia is somewhat dependent on the race of organisms used. A pneumococcus having a very slight virulence may end in a recovery of the animal without lung lesions, while if the organism is too virulent the animal quickly succumbs to a septicemia, and at necropsy shows only a congestion and edema of the lungs. Lamar and Meltzer<sup>7</sup> were the first to regularly produce a lobar pneumonia in animals, though Wadsworth,<sup>8</sup> eight years earlier, by

<sup>4</sup> Münch. med. Wchnschr., 1909, lvi, 377.

<sup>5</sup> Ztschr. f. Hyg. u. Infektionskrankh., 1912, lxxi, 3.

<sup>6</sup> Arch. Int. Med., 1914, xiv, 8.

<sup>7</sup> Jour. Exper. Med., 1912, xv, 133.

<sup>8</sup> AMER. JOUR. MED. SCI., 1904, cxxvii, 851.

carefully balancing the general resistance of the animal with the virulence of the race of pneumococci employed, and by injecting the organism intratracheally, produced in a series of rabbits a diffuse exudative inflammation like the acute lobar pneumonia seen in man.

Wollstein and Meltzer by the use of other organisms, such as streptococcus and influenza bacillus, produced on all occasions a diffuse lesion which resembled closely that seen in bronchopneumonia.

An important factor in the production of pneumonia in animals is the number of organisms which are used. Even in susceptible animals a considerable number of virulent organisms is necessary to produce an infection. Gillespie<sup>9</sup> carried on some important experiments which have a bearing on this problem of why, when a considerable number of virulent organisms is injected, there is multiplication and infection, while if only a few organisms are injected they fail to multiply. It has long been recognized that in starting a culture of pneumococci in broth the number of organisms used depends upon the amount of culture media. For instance, an ordinary loopful of pneumococci might be sufficient to start a growth in 10 c.c. of bouillon, and result in failure if a liter of bouillon were used. Even on serum agar the growth is more rapid and profuse if a stab into the culture is made and the smear started from this point. If the culture is made in a solid media, one organism probably produces a colony. Gillespie was able to show that if the inoculation were made on filter paper kept constantly wet by bouillon, a growth would occur with an inoculation of as small a number of organisms as is required in agar and with a much smaller number than is required to inoculate the bouillon. The conclusion was drawn that for growth to occur the pneumococcus must change the medium immediately surrounding it, and that where diffusion is great the local changes cannot be kept sufficiently constant unless there is a considerable number of organisms in close proximity. This observation has an important bearing on the production of pneumonia. It is not considered that in order to produce pneumonia any such number of pneumococci must be introduced into the infantile being as was necessary to cause a pneumonia in the animals experimented upon by Lamar and Meltzer, but it does appear to be reasonable to suppose that if by any process a few of the terminal bronchioles are occluded, forming a small closed cavity, that pneumococci would be in a situation favorable for their multiplication. According to Cole,<sup>10</sup> extension of the process apparently takes place, in adults, at least, from one lobe to another through the bronchi, as the study of large sections through lobes with beginning involvement shows. It is common knowledge that

<sup>9</sup> Jour. Exper. Med., 1913, xviii, 584.

<sup>10</sup> Loc. cit.

pneumonia in children in a large number of instances follows after a few days of coryza, cough, and not infrequently a bronchitis. It may well be that conditions of this nature, extending along the bronchi, produce a favorable environment for the growth of pneumococci, which, as may be seen from the following table, are so frequently present in the upper respiratory tract of children.

TABLE IV.—PLATE CULTURES OF NON-PNEUMONIA CASES SHOWING TYPES OF ORGANISMS PRESENT.

	Age	Pneumo- coccus	Strepto- coccus hemolytic	Strepto- coccus viridans	Staphylo- coccus
Regulation of diet	4 mos	—	—	—	—
" "	2 mos	—	—	—	—
" "	14 wks	—	—	—	—
" "	16 mos	—	—	—	—
" "	7 wks	—	—	—	—
" "	1 mos	—	—	—	—
" "	4 mos	—	—	—	—
" "	10 wks	—	—	—	—
" "	4½ mos	—	—	—	—
" "	5 wks	—	—	—	—
Malnutrition	3 mos	—	—	—	—
Tertian malaria	12 mos	—	—	—	—
Hypertrophied tonsils and anemia	31 mos	—	—	—	—
Acute intestinal toxemia	2½ yrs	—	—	—	—
Tuberculous peritonitis	24 mos	—	—	—	—
Chronic endocarditis	5 yrs	—	—	—	—
Regulation of diet	12 mos	—	—	—	—
Empyema	3½ yrs	—	—	—	—
Pneumonia	4½ yrs	—	—	—	—
Rickets	1½ yrs	—	—	—	—
Otitis media and rickets	22 mos	—	—	—	—
Pyelonephritis	24 mos	—	—	—	—
Hospitalism	1 mos	—	—	—	—
Eczema	15½ mos	—	—	—	—
Von Jaksch pseudoleukemia	3 yrs	—	—	—	—

The table shows the results of plate culture of sputum in blood agar. Where necessary the pneumococcus findings were verified by inoculation into mice, but, as a rule, the color of the colony, the morphology, and the action of bile upon the organism served to identify it. The specimen was nearly always taken from the upper part of the larynx with a bent applicator. In addition to this series, in which the lung, with one or two exceptions, was free of any known lesion, smears were made from 23 cases of lobar pneumonia in which the sputum was virulent for mice. In all of these a Gram-positive diplococcus was found, and in nearly every case it was the predominating organism, with a few scattered streptococci and staphylococci. In 10 cases of mild bronchopneumonia, the sputum of which did seem to be virulent for mice, the predominating organism was in 5 cases streptococcus; 2 cases each of staphylococcus and influenza bacillus; and in 1 case, tuberculosis bacilli with other organisms.

A few pneumococci were found in four of the series of bronchopneumonia studied, and it is possible that if a larger or more char-

acteristic specimen found could have been obtained that the sputum would have been found virulent for mice.

There were 8 cases of bronchopneumonia in which the sputum was virulent for mice, and in all of these a large number of pneumococci were found in the smears. There were, in addition, however, many other organisms, chiefly of the streptococcus and staphylococcus groups, so that these infections could be fairly labelled as mixed infections. These findings would explain in a measure the difference between a bronchopneumonia and a lobar pneumonia—the bronchopneumonia being a mixed infection, or an infection chiefly with a single type of organism other than the pneumococcus. For this reason the inflammation is peribronchial in character and consists primarily of an infiltration of interstitial tissue with leukocytes. The exudate into the alveoli is moderate and contains little or no fibrin. In lobar pneumonia the inflammation is due chiefly or entirely to the pneumococcus and is not peribronchial in character, and the framework of the lung is free of infiltration. The exudate is considerable and contains a large amount of fibrin. According to Wollstein and Meltzer, slightly virulent or non-virulent pneumococci produce an exudate that resembles that of a virulent streptococcus in the small amount of fibrin present in the exudate.

The question naturally arises as to why infection occurs at all. It has just been shown that pneumococci were found by cultural methods in approximately 25 per cent. of the throats of small children examined in a routine manner in our wards (lungs free). There is no evidence to show that the organisms normally in the throat differ from those which cause pneumonia. There is considerable evidence that different races of pneumococci vary in their virulence toward animals. But the fact remains that some of these organisms which have little virulence for animals have been recovered from cases of severe pneumonia. Whether the resistance to pneumococci has temporarily been lowered in these patients sick with pneumonia is a speculative question to which no reply has apparently been made. It may be believed that the infection is the result of a combination of circumstances, such as the natural or acquired resistance of the individual, the state of the vitality of the individual, local changes in the respiratory tract which precede the infection, and, finally, the virulence of the organism.

Dochez and Gillespie,<sup>11</sup> in their important study, have been able to show that the pneumococcus is a family, which, by the extraordinarily specific methods developed from the study of immunity, can be subdivided into many races having varying degrees of virulence. They liken their subdivision of the family of pneumococcus to other grosser methods of classification, such as differ-

<sup>11</sup> Jour. Amer. Med. Assn., 1913, lxi, 723.

ences in growth or cultural characteristics that are sufficient in certain groups of organisms for differentiation. From the etiological stand-point they do not consider these fine lines of division as important, but from that of specific therapy these differences are of primary importance. At the Rockefeller Institute, under the direction of Dr. Cole, they began in 1910 to use an immune serum that was prepared by injecting a horse with a culture of pneumococcus obtained from Professor Neufeld, the same race he had used in the production of his immunized serum. The protective power of this serum for mice was found by Dochez<sup>12</sup> to be effective in only about one-half the cases. A biological classification of pneumococci was then undertaken by Dochez and Gillespie.<sup>13</sup> Rabbits were immunized to each race of pneumococci, and the protection afforded by these different rabbit serums against all other races of pneumococci was determined.

A considerable number were found to show cross-protection, that is, a serum prepared by injections of one of the number acted on all the races of this group. A horse was then immunized to one of this group and the serum was called Serum No. 2. In this way the pneumococci obtained from all cases of pneumonia were separated into four groups.

Group I contains all those races against which Serum No. 1 is effective.

Group II contains all those races against which Serum No. 2 is effective.

Group III consists of all the organisms of the so-called *Pneumococcus mucosus* type. The individual organisms show a voluminous capsule containing medium-sized, closely approximated cocci with definitely round ends. They produce a sticky exudate in animals and on solid media a moist, transparent mass.

Group IV includes all the cases against which Serum No. 1 and Serum No. 2 are not effective and which from their other properties do not belong in Group III. This group seems to consist of entirely isolated individuals, the significance of which it is difficult to interpret according to Dochez. It may be that this heterogenous group may be representative of the type of pneumococcus found in the normal mouth.

In our experiments there were obtained eleven strains of pneumococci from the throats of children having no lung involvement all of which belonged in Group IV. In one case pneumococci of Group I were obtained before physical examination revealed a lobar pneumonia.

The chief difficulty met with in babies and small children was the obtaining of a sufficient specimen for a direct mouse injection. The method which was finally adopted was a simple one, con-

<sup>12</sup> Jour. Exper. Med., 1912, xvi, 680.

<sup>13</sup> Jour. Amer. Med. Assn., 1913, lxi, 727.

sisting of a tongue depressor, placed well back on the tongue and down in the throat. This method resulted in some gagging and more or less coughing, which in most cases brought a plug of mucus up into the throat, which was caught on the spatula. While the amount obtained was often scanty, only occasionally was it necessary to take a second or a third specimen. The method used from this point closely follows Dr. Cole's description of the method used at the Rockefeller Institute. The sputum was immediately injected into the peritoneal cavity of the mouse. The peritoneal cavity was washed with salt solution as soon as the mouse showed symptoms of being severely ill. The cells were thrown down in a centrifuge, a suspension of the organisms being thus obtained. The agglutination test was at once made with Serum No. 1 and Serum No. 2.

At the same time that this was being done a very small amount of blood was withdrawn from the heart and smeared across a blood-agar plate. In twenty-four hours the type of colony can be studied on the plates and further agglutination or cultural tests made. The work was checked by a Gram and a capsule stain (His's method) and by lysis of the bacteria with bile. In making the agglutination tests from the peritoneal washings the amount used depended somewhat upon the opacity of the solution containing the suspension, and 0.3 c.c. of the serum was the amount employed.

Our final test was always made with an eighteen-hour-old broth culture inoculated from typical plate colonies. Equal amounts of the broth and serum were employed in the test (as a rule, 0.3 c.c. broth culture and 0.3 c.c. of serum). It was noted that a fairly high dilution of the serum often made it difficult to obtain an agglutination; but, as a matter of fact, the organisms seem to have the property of remaining suspended in the serum used, even though the serum was not diluted at all. Readings were made macroscopically at the end of one and two hours at 37° C., and again after standing twenty-four hours in the ice-box. Usually, agglutination was visible in fifteen minutes or half an hour, and consisted at first of a fine granulation followed by a sinking of clumps which form a thin layer on the bottom of the tube that could not be broken up even by vigorous shaking.

The serum for Groups I and II was obtained through the kindness of Dr. Cole, at the Rockefeller Institute. Somewhat to our surprise, for we expected many of our pneumonias to fall into Group IV, our cases paralleled quite closely those at the Rockefeller Institute so far as groups are concerned. We obtained many more in Group II than Dr. Cole's published results would seem to warrant; but in a personal communication, Dochez has told us that he too had an unusually large number of organisms fall into Group II during the past winter. The following table briefly summarizes our results:

	Cases of lobar pneu- monia.	Cases of broncho- pneu- monia.	Prim- ary.	Second- ary.	Deaths.	Cures.	Total number of cases.	Percentage in each group (cases with no results not included).	Per cent. of mor- tality.
Group I	9	2	9	2	1	10	11	22.9	9
Group II	11	3	12	2	5	9	11	29.3	36
Group III	1	3	2	2	1	3	4	8.3	25
Group IV	7	12	6	11	4	15	19	39.8	21
No result	3 <sup>14</sup>	12	..	..	..	..	23 <sup>15</sup>		
Total	..	..	..	..	..	..	71		

It will be noted that there are 48 cases in which it has been possible to determine the group to which the pneumococcus causing the infection belongs. Of the 23 cases in which it was not possible, for one reason or another, to obtain a pneumococcus culture, in at least 3 a positive result would in all probability have been obtained with a proper specimen. Empyema occurred as a complication in 7 of these cases. With one exception, the organism recovered from the empyemas was the pneumococcus, of which 2 belonged in Group I, 3 in Group II, and 1 in Group IV. The seventh case gave a pure culture of *Streptococcus hemolyticus*.

Our mortality-rate for the groups, with the exception of Group IV, is somewhat lower than in the series published by Cole.<sup>16</sup> For purposes of comparison, mortality percentages for the two series are placed side by side.

	Our series.	Cole's series.
Group I	9 per cent.	24 per cent.
Group II	36 "	61 "
Group III	25 "	60 "
Group IV	21 "	7 "

The number of cases in both series is as yet insufficient for the determination of the absolute mortality rate in each group. As our series is based on children under six years of age, a comparison with Cole's adult cases is obviously unfair. Lobar pneumonia decidedly predominated in Groups I and II, while rather more than half the cases in our Group IV were clinically bronchopneumonia, while the cases dealt with by Dr. Cole are exclusively of the lobar type. Moreover, there is an actual difference in the mortality-rate in the two series, ours being 23 per cent., as opposed to Dr. Cole's 38 per cent. In all probability this marks another difference in the two series, as we used every pneumonia case that came into our children's service, while probably only very ill patients were sent to Dr. Cole's service at the Rockefeller Institute.

SUMMARY. From a study of a thousand cases we have established a mortality-rate for pneumonia of 34.3 per cent. It is admitted that this is probably a higher rate than obtains in private practice

<sup>14</sup> Two cases sputum taken after all symptoms had disappeared.

<sup>15</sup> Eight of these were control cases, having no lung involvement.

<sup>16</sup> Loc. cit.

among well-to-do people, but is the average for the mass of city dwellers in this locality. Bronchopneumonia is preëminently a disease of the first two years of life, and after the third year is relatively uncommon. Lobar pneumonia is the type of the disease which is present after the third year in practically all cases of pneumonia, if those cases which are frankly secondary to some other condition, such as one of the infectious diseases, or where the pneumonia occurs as a terminal infection, are omitted. Lobar pneumonia *per se* is a common condition in the first and second years of life, being much more frequent than is commonly supposed. The infection which is the etiological factor of lobar pneumonia is always the pneumococcus, while a bronchopneumonia may be due to a number of organisms, such as the streptococcus or the influenza bacillus, occurring alone or as a mixed infection. If pneumococci are present in bronchopneumonia they are usually one of a group of various organisms, or at least are of a low virulence, and resemble the organisms commonly found in the mouth. The pneumococcus may be divided into four general groups, each being made up of many races which are closely related. By the method outlined a pure culture of pneumococcus may be obtained and the group determination completed in about twenty-four hours from any given case of pneumonia. The division of the pneumococcus into groups is of the greatest importance from the stand-point of treatment. Obviously the treatment of a lobar pneumonia due to a pneumococcus of Group II with a serum or vaccine prepared from an organism of Group I is a waste of energy and might be positively harmful in its effect.

Pneumonia is the most common, is the most fatal, and is the least studied disease that occurs among children. Any work which brings new facts relating to its treatment or new possibilities of improved methods and prevention is worthy of the careful consideration of all those who are interested in the welfare of children. It is hoped that the division of pneumonia into groups will eventually bring about the treatment by specific sera or vaccines, replacing the symptomatic treatment of today.

### ACUTE CEREBELLAR ATAXIA IN CHILDREN: REPORT OF A CASE, WITH RAPID AND COMPLETE RECOVERY.

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THE condition about to be described appears to be an uncommon one. On this account it seems well to put the following case on record and to review the already published cases of a similar nature,



Susie R., aged five years. The family history showed nothing of importance. There were three brothers and one sister, who were well. The patient had always been a healthy child, except for occasional attacks of bronchitis. There had been no illness of any sort in the household recently. On Monday, January 4, she suffered from cold in the head and a bronchial cough. An epidemic of influenza had been prevailing in the city. The symptoms continued upon Tuesday, January 5, although the child was running around as usual. On Wednesday, January 6, she was worse, and Dr. Wm. McCombs attended her for the next several days, and put her to bed. She had a heavily coated tongue, headache, and a temperature from  $98^{\circ}$  to  $102^{\circ}$ . She continued about the same from January 7 to January 9, when her temperature had become normal. By Sunday, January 10, she was apparently quite convalescent, and was allowed to get out of bed. This day she was cheerful, playing, and seemed entirely well. In the evening, however, she complained of slight earache, from which she had never suffered before, but on Monday, January 11, she was up and about. Toward evening she began to complain that her hip hurt her, and she was hardly able to walk. On Tuesday, January 12, she vomited before she was out of bed. Later in the course of the morning she got up, but in the afternoon vomited several times and went back to bed. She still complained of her hip hurting, and any pressure upon it seemed to make her shake all over. The mother noticed also that there was a jerking, irregular character to her speech. These were the first distinct nervous symptoms, and her mind seemed entirely clear. On the morning of Wednesday, January 13, the child was scarcely able to stand, and the mother now noticed the irregular movements of the eyes and eyelids. On this day she seemed dazed. Dr. McCombs described it as "a state of fear." She could not well be quieted, and in the afternoon her mental state became worse, and in addition she could not sit unsupported. About 9 o'clock in the evening she began to scream violently, sometimes for an hour at a time, almost without pause. This continued until 4 o'clock on the morning of the next day, January 14. She was pale and trembling; half delirious; there was apparently no disturbance of the tactile sensation, and she could feel wherever she was touched. After about two hours' sleep she started to scream again, and was taken during the day to the Children's Hospital, four days after the onset of the acute symptoms.

Examination on admission, January 14, showed a well-nourished child of good color. The mind did not appear entirely clear, but there seemed to be no special excitability. She could utter a few words, but with great difficulty, and the speech was very jerking and irregular. There was a very high degree of lateral nystagmus nearly always present, but growing worse in paroxysms and increased on ocular exertion, and accompanied by a fluttering move-

ment of the eyelids. The patellar reflexes were increased. There was a decided incoördination of the muscular movements of the extremities. A few mucous rales were heard in the lungs; respiration was regular. The heart showed nothing abnormal.

I made an examination of the child for the first time upon the next day, January 15, with the following notes: "The mental condition must certainly have improved, for it now seems nearly normal. She answers questions clearly, but after some delay and with a slight trembling of the voice. There is a curious, very marked fluttering of the eyelids which is not constant; and with this a rapid nystagmus, both lateral and vertical, lasting for a moment and then for a moment disappearing. No paralysis of the ocular movements can be found, and no facial paralysis. The child can whistle and show her teeth when directed. Her grip is good. There is trembling and a very decided ataxia in the movements of the arms and of the hands on attempted effort, apparently not increased by closing her eyes. The patellar reflexes are active, and there is slight ankle-clonus of the right foot, and a suspicion of this in the left foot. The Babinski symptom is absent. She can stand only when supported, and with her feet broadly separated from each other."

On January 16 and 18 Dr. Isaac Jones made careful examinations of the ears to determine whether the nystagmus was otitic in origin. The summary of his report reads as follows: Typical nystagmus and unbalancing of the control of the eye-muscles are present. This is not due to any lesion of the ear, or any disturbance of the vestibular apparatus, because (1) spontaneous nystagmus on looking to the extreme right or left is decreased instead of increased; (2) the hearing is normal; (3) stimulation of the semicircular canals gives the correct normal nystagmus, controlling the oscillations and converting them into rhythmic nystagmus of a vestibular character, with a slow and rapid component. The nystagmus-circuit is, therefore, intact on both sides; indicating normal semicircular canals, eighth nerves, region of Deiters' nucleus, the posterior longitudinal bundle in the pons and its connection with the third and fourth nuclei, and, finally, the third and fourth nerves themselves.

On January 19 an ophthalmological examination was made by Dr. H. M. Langdon and the following report rendered: "Palpebral fissures about equal. In the right eye the pupil measures 4.5 mm.; left eye, pupil slightly smaller. On admission of light the accommodation is normal in each eye. The ocular rotation seems full and equal in all directions, the visual axes being parallel. The eyes are steady on fixation, but on rotation in any direction there develop a few quick nystagmic jerks, usually about five or six oscillations in a group, and then steady fixation will be resumed. The movements were usually accompanied by curious fluttering

of the eyelids. The disks are slightly full, normal in color, with clear margins. There are no changes of the fundus."

Improvement went on with great rapidity. By January 23, nine days after admission, the child could sit up in bed unsupported, with some ataxic movements of the arms on attempting to balance herself. While standing on the floor there were some oscillatory movements of the entire body, but she could now walk if supported by one arm, and her gait was normal, except for a degree of weakness and uncertainty. On closing her eyes she was unsteady, but not to a degree constituting Romberg's symptom. The grip was only fair, but equal on both sides. The patellar reflexes were slightly increased on the left side. No ankle-clonus or Babinski reflex was present. The eyes exhibited a rotary nystagmus as observed before, but to a much less degree. The sensorium was entirely normal; the child answering questions and conversing freely, in contradistinction to the condition earlier in her history, when, although she would answer questions, she made no effort to speak at other times. The tongue was protruded with ease in any direction. No facialis symptom could be elicited. She complained of her feet being constantly cold. She could feed herself fairly well and touch her nose with the eyes closed.

By February 1, seventeen days after admission, it was noted that she still walked with some unsteadiness, but without any support, and with the feet rather wide apart and the body bent somewhat backward in the effort to balance herself. The nystagmus had disappeared except on continued ocular exertion to the extreme of the ocular field. On February 10, one month after the onset of the acute symptoms, she was discharged from the hospital, and the following note was made: "Since admission there has been an entire change of mentality from sluggishness, haziness, and dullness to a condition of alertness and brightness."

The temperature while in the hospital was afebrile, except for a rise to 100° on a single occasion. The Wassermann reaction taken on January 18 was negative and the von Pirquet faintly positive. Lumbar puncture on January 21 gave a dry tap. The urine was examined on a number of occasions, and was practically always negative. On one examination a faint trace of albumin, cylindroids, an occasional hyaline cast, and a few leukocytes were reported. Examination of the blood on the day of admission showed a leukocyte-count of 11,600. The differential count gave polymorphonuclears, 57 per cent.; lymphocytes, 31 per cent.; mononuclears, 7.5 per cent.; transitionals, 3 per cent.; eosinophiles, 1.5 per cent.; basophiles, 0.

Treatment consisted on admission in the administration of a purgative and of sodium bromide. After this, on the ground that the condition might be toxic, bicarbonate of soda was given every four hours and enteroclysis every six hours. This treatment was continued until recovery was well advanced.

The noteworthy features in this case consist in the rapid development of symptoms without discoverable cause, unless possibly the child had suffered from influenza; the very uncommon degree of nystagmus; the ataxia of the extremities; disturbance of sensorium; affection of speech; slight increase of reflexes, and the rapid recovery, complete in one month from the onset.

We have here symptoms which, on the whole, point chiefly to some disorder of the cerebellum. That this was the only portion of the brain affected would seem questionable. As Batten<sup>1</sup> has pointed out in an able paper upon "Ataxia in Childhood," it is impossible to draw a sharp line between the cerebellar and the cerebral cases. In some the symptoms pointing to cerebral involvement predominate, and in others, as in the case reported, the cerebellar symptoms are in the ascendency.

In the case I have described, such systemic disorders as Friedrich's ataxia and the cerebellar ataxia of Marie were naturally out of the question. Tumor and abscess of the cerebellum, at first thought to be possibilities, were excluded by the course of the disease and by the examination of the eye-grounds; and that the nystagmus was not otitic in origin was shown by the application of Bárány's tests, although this was not certain proof that the symptom depended upon a cerebellar lesion.

Fickler<sup>2</sup> gives a convenient classification of the diseases of the cerebellum, which may profitably be considered in the effort to place the case described. The first group is that of congenital cerebellar ataxia, from which this case is naturally excluded by the age. The second consists of the acquired cases, which are subdivided into the chronic progressive and the acute forms. The latter, to which this patient naturally belongs, is again divided into (*a*) traumatic (*b*) encephalitic, and (*c*) toxic. According to this classification the encephalitic cases follow especially the infectious diseases. The toxic cases would be represented in early life by those depending upon gastro-intestinal auto-intoxication. The anatomical difference would appear to be that in encephalitis there is an actual inflammatory process active, and in the toxic cases the condition in the acute stage is one of cellular degeneration. Clinically it would seem difficult to make a sharp distinction, and the two may be conveniently grouped in this connection under the heading of acute non-suppurative encephalitis, or acute hemorrhagic encephalitis.

The acute infectious diseases are the most frequent of the causes mentioned. In epidemics of poliomyelitis, too, cases are not infrequently seen with the symptoms of encephalitis, alone or in combination with spinal symptoms. The process in this disease is known to be an inflammatory one; and yet the recovery may be

<sup>1</sup> Brain, 1905, xxviii, 484.

<sup>2</sup> Deutsch. Zeitschr. f. Nervenheilk., 1911, xli, 306.

so complete in some instances that, in the absence of any other satisfactory explanation, the case recorded here might perhaps be assigned to this group; in this instance, most unusually, the cerebellum bearing the brunt of the attack. Against this supposition, yet not completely excluding poliomyelitis as the etiological factor, is the fact that nearly always the lesions in this condition are more widely disseminated than in the present case.

In the large majority of cases of uncombined acute hemorrhagic encephalitis the process is limited to the motor region of the cerebrum. In many it is seen also in, and in a very few cases it is confined entirely to, the region of the pons and medulla. In other cases, much less numerous than the first class, the encephalitis, as stated, attacks especially the cerebellum. In this event there is the comparatively sudden development of the symptoms of encephalitis in general, such as fever, unconsciousness, convulsions, and the like, lasting a variable time, although in the end the cerebellar symptoms predominate. The most characteristic of these are ataxia, staggering gait, and vertigo; although often associated, but not certainly cerebellar in origin, are nystagmus, disturbances of speech, and tremor.

The prognosis of the great majority of cases of acute non-suppurative encephalitis, whatever the location, is favorable as far as life is concerned, and favorable, too, as regards improvement; but less so as regards complete recovery of power and of a normal mental condition.

Batten details several cases similar in many respects to the one I have reported, and publishes others collected from medical literature; and there are still a number of others not found in his series. I append abstracts of all the cases I have been able to discover. Only those are included in which the course of the disorder was sooner or later arrested and improvement followed. Those showing a progressive increase in the symptoms do not belong to this category.

(1) Shepherd (*Med. Times and Gazette*, 1868, i, 144). Girl, aged five years. On the second day of scarlet fever she became speechless. Examination a month later showed her unable to speak, write, or stand; her head and arms fell forward; her legs were weak. After three weeks she improved rapidly and could walk, although with an ataxic gait. Gradually she became more intelligent. In about three and one-half months from the onset she could play about the ward, although her movements and speech were far from normal.

(2) Schepers (*Berl. klin. Wchnschr.*, 1872, ix, 517). Girl, aged eight years. On the fourth day of measles she became unconscious, and later exhibited aphasia and then marked ataxia of the limbs. The intelligence seemed unaffected; the sensibility normal. In one and one-half months she began to speak, but with an altered

voice; she could stand supported, but not walk; there was great ataxia in the hands. A week later she walked with an ataxic gait. Memory had been largely lost, but she learned rapidly, and several months later rejoined her original class in school. Schepers speaks of the favorable outcome, but does not state whether any traces of the disorder remained.

(3) Feith (*Allg. Zeitschr. f. Psychiat.*, 1873-4, xxx, 236). Boy, aged five years. Typhoid fever was followed by aphasia, ataxia, and unconsciousness. After three weeks improvement took place in the mental state, but he still could not stand. Later he had psychic disturbances and a distinctly ataxic gait, and this condition lasted three weeks. About two months after the onset he seemed to have recovered completely. No reference is made to any ataxia of the upper extremities.

(4) This case is the only one in the series following trauma. The question could be raised whether it should properly be included here, inasmuch as the ataxia was of slower development than in the other instances. It seems to me, however, rapid enough to be called acute;—

Bastian (*Lancet*, 1878, ii, 207). Girl, aged ten years. She fell down stairs striking the occiput; experienced no loss of consciousness, but suffered from pain in the head on the next day. Two weeks later she had another fall on the occiput. After this she grew worse, and in two weeks was having vomiting and occipital pain. She was sent to the hospital eight weeks after the first fall. One week later, when attempting to get out of bed, she was found to stagger badly. Soon after this the sight became impaired. When seen again six months after the first accident she had a drunken gait; incoördination of the hands; optic neuritis; pain in the head; normal intelligence. She grew worse for a time, but after about three months improvement began, and in two months more she had perfect power in the upper extremities. By about a year after the fall she was entirely well, except a slight affection of gait.

(5) Lenhartz (*Berl. klin. Wchnschr.*, 1883, xx, 312). Boy, aged eight years. Acute dysentery was followed promptly by a brief maniacal state, and then entire loss of speech; anesthesia; paralysis of the sphincters, and mental weakness. Two weeks later he had nystagmus and marked ataxia of the head, extremities, and trunk. The aphasia and ataxia lasted for months, and he could not speak for three months. At the end of two and a half years there was only a little ataxia and slowness of speech and a deficiency in intelligence.

(6) Hammarberg (*Nord. med. Arkiv.*, 1890, xxii, No. 23). Male, aged seven years when he had pertussis, and soon after this "inflammation of the brain," with unconsciousness for a short time. This was followed by rhythmic swinging movements of the head; incoördination of the arms; loss of speech; inability to walk, and mental

disturbance for a short time. The condition remained unchanged for three months and then gradually improved. About one year after the onset the ataxia had lessened and he could walk unaided, but the gait was uncertain and reeling. The patient finally returned to school, but his gait continued to be always uncertain; the speech scanning and slow; he could not write well, and his disposition was altered for the worse. At the age of twenty-two years he had inflammation of the lungs, and after this gradually became insane and died at the age of twenty-four years.

(7-9) Lütjje (*Deutsch. Zeitschr. f. Nervenheilk.*, 1902, xxii, 280). Three cases occurring in one family, all developing during severe typhoid fever.

(7) Boy, aged ten years. Unconsciousness developed on the fifth day of the fever. This persisted for seven weeks, and afterward he remained dazed for over a month more and could not speak. During this time there were rhythmic movements of the head. When discharged from the hospital, four months after the onset, he could walk only with support; had ataxic movements of the legs and of the left arm; disturbance of speech, and ataxic nystagmus.

(8) Girl, aged seven years. Had unconsciousness for weeks, with oscillatory movements of the head, grinding of the teeth, and twitching of the face. She gradually improved and then showed decided ataxic movements of the extremities. Two and one-half months after the onset there were still imperfect speech; marked ataxia of extremities; unsteady gait; active tendon reflexes, and ankle-clonus. The sensibility was not affected, and there was no nystagmus or psychic disturbance. Three weeks later the gait and speech were still affected, but the upper extremities were normal.

(9) Boy, aged six years. He had a dazed condition for one and one-half months, and did not speak for two weeks more. Meantime there were rhythmic movements of the head, and marked ataxia of the trunk and extremities. No effort to speak was made until after one and one-half months, and then the speech was slow and scanning. He improved rapidly, and about two months from the onset he had remaining only a slight disturbance of speech and of gait.

Lütjje summarizes the principal symptoms of all three cases as follows: Severe typhoid fever followed by unconsciousness lasting for weeks; gradual recovery of mentality; severe ataxia in all the muscle groups, without paralysis or disturbance of sensation; slight disturbance of intelligence affecting the memory; scanning speech and increased reflexes.

(10) Taylor (*Lancet*, 1904, ii, 1416). Boy, aged four years. Six weeks before he was admitted to the hospital he had a slight fall, but without striking the head; three weeks later he had pertussis; four days before admission he developed twitching of eyes,

hands, and feet, and was unable to walk. Examination showed trembling of the limbs and the trunk, suggesting disseminated sclerosis; inability to speak plainly or to walk alone; nystagmus. In twenty-two months he could walk with a drunken gait when supported; the arms were ataxic; the speech hesitating; the mental condition good. By three and one-half years after the onset he was reported to be nearly well, although the speech was still a little imperfect. Examination over twenty years later showed the recovery complete.

(11) Voelcker (*Brain*, 1905, xxviii, 360). Girl, aged four and a half years. Scarlet fever was followed by unconsciousness lasting two weeks; no vomiting. Then the speech was found to be lost and she could not feed herself. Improvement gradually followed and when examined three months later she could not stand; the gait was ataxic when supported; there was some ataxia of the upper extremities; tremor of the head; brisk knee-jerks; variable plantar reflexes; no ankle-clonus; slow and indistinct speech. Two months later (five months after the onset) she showed little improvement; the knee-jerks were less active; the ataxia less; the mental condition improving. One and a half months after this the symptoms were still very marked.

(12) Guthrie (*Brain*, 1905, xxviii, 363). Girl, aged seven years. During measles there occurred vomiting, convulsions, squint, and unconsciousness. After five days she was better, but could not speak. Aphasia persisted, and there developed exaggerated knee-jerks; incoördination of upper and lower extremities; anesthesia and loss of sphincter-control. She improved gradually, and in three months could stand, talk, and feed herself. Sixteen months after the onset there were drawling speech; slight ataxia; tremor of the upper extremities; ataxic gait; brisk knee-jerks; ankle-clonus at times. She was mentally slow.

(13) Batten. First case. (*Brain*, 1905, xxviii, 489.) Girl, aged four and a half years. Immediately after influenza she developed vomiting, and in a week paresis of the legs and affection of speech; slight involvement of the sphincters; no loss of consciousness and never headache. A month and a half later she showed a wildly ataxic gait when supported, and could barely stand alone. There were marked incoördination of the hands; somewhat bulbar articulation; slight paresis of the left side of the face; active knee-jerks; doubtful ankle-clonus. There was no nystagmus. Examination three months after this showed that recovery was complete.

(14) Batten. Second case. (*Ibid.*, 490). Boy, aged three and a half years. Measles was followed by convulsions and unconsciousness lasting a week. Two months later there were slow speech; marked ataxia of the arms and legs; slight ankle-clonus, and perverted moral sense. There was no nystagmus. After one and a half years he was very much better. When seen last, April, 1907



(*Clin. Soc. Trans.*, 1907, xi, 276), there was still slight incoördination of the legs, although the gait was good; the speech was rather slow and hesitating, and the mental condition rather backward for the age.

(15) Batten. Third case. (*Clin. Soc. Trans.*, 1907, xi, 276). Boy, aged eleven years. Without known cause he developed headache and on the next day falling; inability to feed himself, and vomiting. On the sixth day he had a drunken gait; ataxia of both legs, but less in the hands; nystagmus; active knee-jerks; loss of tone in the limbs; no affection of sensation. He improved rapidly and in a little over three weeks showed only slight ataxia of the lower extremities.

(16) Batten. Fourth case. (*Ibid.*, 277). Boy, aged twelve years. He had had petit mal for some years. After a severe attack he suffered from unconsciousness for three days. Following this there were no control over the arms or legs; slow and jerking speech; unsteadiness of the trunk and head; poor mental condition; intention-tremor; no vomiting or headache. He had not been able to walk for over six months, and when aided had a wildly ataxic gait. The knee-jerks were active. He improved but little while under observation.

(17) Nonne (*Neurolog. Centralbl.*, 1909, xxviii, 885). Boy, aged twelve years. During an epidemic of poliomyelitis he developed an encephalitis with cerebral symptoms, especially Jacksonian epilepsy, and subsequent hemiplegia. He was unconscious for a week. After subsidence of the cerebral symptoms, he showed general disturbance of coördination, affecting even speech and the muscles of respiration. In the course of two months the symptoms subsided, and in three months he was completely well.

Among more than doubtful cases not included in this series may be mentioned the following:

Marie and Joltrain (*Rev. Neurolog.*, 1910, xx, 123). Boy, aged fourteen years. He had typhoid fever at five years, followed by difficulty in speech, in walking, and in some of the movements of the extremities. The condition steadily grew worse. There was marked ataxia with complete abolition of reflexes. The mental state was normal.

This case, although beginning apparently acutely, had shown such a progressive increase of symptoms that it is rather to be placed in the category of "chronic progressive ataxia."

Baudoin and Français (*Rev. Neurolog.*, 1910, xx, 139). Girl, aged seven and a half years. Epileptiform seizures began at three months and continued with irregular and increasing frequency. When examined by the writers at seven and a half years of age the intelligence was little developed; she could express herself very imperfectly; there were slight increase of the knee-jerks on the left side; some hesitation and trembling in the upper and lower extremities, and a cerebellar gait. There was no nystagmus.

The doubt in this case is principally as to the acuteness of the origin, which may, in fact, have been congenital.

Williamson (*Proc. Royal Soc. of Med.*, 1912-13, Section on Diseases of Children, 41). Boy, aged ten years. Tremor began three and a half years before, and the child lost strength and grew less bright. Examination when brought to the hospital showed tremor in the arms and tongue; ataxic gait; brisk knee-jerks; no nystagmus. Seven months later there had been no marked progression of symptoms. A doubtful slight lateral nystagmus was present.

Williamson says that juvenile paralysis could be thought of in the diagnosis. There is nothing in his history indicating an acute onset, and the case hardly belongs here.

The following analysis and conclusions may be formulated based upon the 18 cases, including my own. They are necessarily incomplete, owing to the absence of sufficiently full details in some instances.

The immediate apparent causes of the attacks in the cases as reported are divided into scarlet fever, 2 cases; measles, 3; typhoid fever, 4; pertussis, 2; influenza, 1; poliomyelitis (?), 1; epileptiform convulsions, 1; trauma, 1; dysentery, 1; not discovered, 2. Possibly my own case, placed in the last class, could with reason be assigned to influenza. The preponderance of acute infectious diseases is very evident. Only 1 case followed trauma. It does not appear that the pertussis reported in 2 instances was of sufficient severity at the time to put these cases in the class of traumatism from violence of coughing; but possibly the case following epileptiform convulsions could be placed here. The instance of an attack following dysentery might possibly be an example of ataxia of toxic origin, but the duration was almost too long to permit of this conclusion. Ten of the patients were boys and 8 girls. The age at the time of onset ranged from three and a half years to twelve years, 10 of the patients being six or more years of age.

That the condition present is in fact dependent upon a lesion of the cerebellum is, in a way, an assumption. Only in the patient seen by Hammarberg did the case come to autopsy, and here very serious alterations of the cerebellum were found. This, however, was years after the first appearance of symptoms, the patient meanwhile having become insane and developing new somatic disturbances; and to how great a degree the early acute manifestations depended upon the lesions found must remain uncertain. The complex of symptoms based upon the composite of all the cases seems sufficient, however, to warrant a belief in the cerebellar origin. That the malady is not dependent upon vestibular or labyrinthine disease was shown in the case now reported by the application of Bárány's tests, and in none of the patients was any impairment of hearing noted. Vertigo, so characteristic a cerebellar or labyrinthine symptom, is not referred to in any of the reports.

The early age of most of the patients makes the identification of this symptom a matter of difficulty.

Disturbances of the sensorium were present in the early states of a large number of cases. Unconsciousness is mentioned in 11 instances, sometimes of brief duration, sometimes lasting for weeks. Convulsions were occasionally seen; delirium was also observed. All these may be classed among the symptoms common to any severe intracranial lesion, or they might be the evidence of a complicating disturbance in other regions than the cerebellum. Some affection of mentality, apart from unconsciousness, was present in 12 instances. In most of these it was of brief duration, but in a few it persisted in some form for a longer time. In such it, of course, indicated lesions elsewhere than in the cerebellum alone. Regarding the disturbance of speech, it is interesting to observe that in 8 cases the patient was for a time entirely unable to speak, and in some instances this condition lasted for months. Later, after the power to speak had been regained, in all but 3 of the cases some affection of it remained for a variable time, and in many was still present when the patient was last seen. It is described as "slow," "drawling," "scanning," "jerking," or "irregular." The affection of speech might with propriety be considered an extracerebellar disturbance, but certainly in some cases at least, and perhaps in most of them, seems not so much to depend upon an involvement of the centres for speech as upon an inability to articulate properly—an ataxic condition. It is possible that in producing the speech-disturbance the medulla may also be involved, and the same is true of the vomiting, which was seen early in some of the cases.

The tendon reflexes were found "brisk" or "increased" in 9 instances. In the others nothing is said upon the subject. Ankle-clonus was present in 4 cases. It is evident, then, that there is a distinct tendency to increase of the reflexes in this disorder, pointing toward the cerebellar involvement. In a few cases "weakness" or "hypotonia" of the limbs is mentioned, but in others it is distinctly stated that no weakness or paralysis was discoverable. In general it is a fair conclusion that the inability to walk or to use the arms depended upon the ataxia rather than upon paresis. The ataxia was noted in every instance; in the legs in all, in the arms it appears to have been present in all but one case. Not infrequently the trunk and the head shared in the incoördination. Anesthesia is mentioned in 2 instances, and more or less loss of control of the sphincters in 3. These symptoms are, of course, not cerebellar. It is to be observed that nystagmus is recorded in but 5 cases; apparently in none of the others as marked as in my own patient. Although it is probable that there exists a cerebellar nystagmus, the symptom is certainly produced by lesions of other regions as well; and this series shows how frequently

there may be a cerebellar ataxia without nystagmus. Optic neuritis was seen in but one instance.

That the lesion is one capable of partial or even complete removal or compensation is shown by the history of the majority of the cases. In 7 it is stated that entire recovery ensued, and it is probable that Scheper's case is to be included here, although the text is not quite clear. In my own patient recovery was complete in one month from the onset of the attack; in Feith's case in two months; in Nonne's case in three months; in Batten's first case the patient was found well in four and a half months. The case of Taylor is of special value from a prognostic point of view. After three and a half years following the onset there were still slight evidences of the disease present, but when seen over twenty years later recovery was complete. In a number of the cases reported the time which had elapsed during which the patient was under observation had been short, and the improvement had been rapid; and it is a fair presumption that many of these recovered completely. There is, indeed, every reason to believe that in most instances few if any evidences of the disease will remain. That, however, severe symptoms may persist a long time and probably always is shown by at least 8 of the cases, and in some of these unfortunately some intellectual or psychic abnormality remained.

### PNEUMOTYPHOID, WITH REPORT OF A CASE.

BY FRANK BILLINGS, M.D.,

CHICAGO, ILLINOIS.

PNEUMONIA during the second and third week of typhoid fever is not a rare event. It then expresses itself in various forms, sometimes frank and outspoken, sometimes obscure. There may be a leukocytosis, more hurried respirations, a higher pulse rate, and evidences of a more toxic condition. The sputa may be swallowed, or may be evident and present the usual characteristics of a pneumonia. The pneumococcus may be found in smears of the sputa, occasionally the typhoid bacillus, and very commonly various strains of the streptococci and indifferent bacteria. In other words, the pneumonia may be that due to the pneumococcus or to many other types of organisms, and often is the so-called septic type.

Pneumonia which expresses itself in the first days of typhoid fever is rare. But few cases can be found mentioned in the literature. MacCrae mentions 3<sup>1</sup> as occurring in the patients treated

<sup>1</sup> Osler's Modern Medicine.

for typhoid fever at Johns Hopkins Hospital. One of these developed gangrene of the lung, and typhoid bacilli were found in the sputa. F. Glaser mentioned<sup>2</sup> a patient who had consolidation of the lower lobe in the early days of typhoid. This patient had bloody sputa, but no typhoid bacilli were found. An empyema resulted, and in the pus from the pleural sac the bacillus of Eberth was recovered. A. Fränkel<sup>3</sup> makes a statement that the primary localization of typhoid bacillus in a lung with the production of pneumonia is clinically unknown.

The subject of this report is of exceptional interest because she presented a frank, outspoken lower-lobe pneumonia in the first days of what proved to be typhoid fever, and the rare occurrence of the clinical type makes it worthy of a report.

The patient was Mrs. S. T., married, born in Greece, aged twenty-three years, was admitted to the Presbyterian Hospital, Chicago, on November 29, 1913. She was unable to speak English, but through an interpreter it was learned she had been ill for about one week. The illness began with a mild chill followed by fever. Chilliness with high fever continued until she was admitted to the hospital. From the beginning of the illness there was moderate pain in the right lower chest. There was moderate cough with a slight expectoration of yellow, tenacious sputa. The patient was weak, without appetite, bowels constipated, and she suffered great thirst. She stated that the illness began suddenly, and until the day of the chill she was able to do her domestic work. She was nursing the younger of two children, born five weeks before the illness began. The patient had been an inmate of the hospital in March, 1912, when she suffered from an acute bronchitis. With this exception she had enjoyed good health since childhood. On admission the patient had the appearance of marked illness—face flushed; eyes bright; respiration rapid; tongue coated with yellowish-brown fur; pharynx dark red; tonsils small, showing crypts containing yellowish plugs; lips and finger nails moderately cyanotic; both mammae full and firm; chest symmetrical; right chest expansion less than left, most marked in the lower portion; a high degree of dullness on percussion over the lower right lobe with increased tactile fremitus and bronchophony; bronchial breathing and crepitant rales heard over the entire lower lobe; heart area of dullness, rhythm, and tones normal; pulmonic second sound accentuated; abdomen, rounded contour, flaccid walls, no tenderness; liver negative; spleen easily palpated. No skin eruption. No herpes of lips. Temperature by mouth 101.2° F., pulse 96, respiration 32. Blood: hemoglobin, 80 per cent. Dare; white-blood cells, 12,900; polynuclear cells, 76 per cent. Blood-pressure, Tycos, systolic 115, diastolic 80. Urine: dark amber; acid; 1.022;

<sup>2</sup> Deutsch. med. Wchnschr., October 30, 1912.

<sup>3</sup> Ibid., March, 1899.

albumin trace; sugar, 0; casts, 0; red-blood cells, 0. Sputa: small amount, viscid, mucopurulent, few pneumococci and streptococci, and indifferent bacteria.

A high fever, of a continuous type, with full pulse of 90 to 100, respirations of 30 to 40, and extension of consolidation to the middle and upper right lobes were the chief clinical characteristics in the next two weeks. On the second day in the hospital the white-blood cells numbered 8700 and on the eighth day 12,000. The patient had been managed up to this time as an ordinary lobar pneumonia, involving finally the entire right lung. Because of its long continuance and of an increase of dulness to practically complete flattening over the posterior portion of the right lower lobe a paracentesis was done in this area without obtaining fluid. Then a blood culture was made on December 15, the seventeenth day in the hospital, which yielded a pure typhoid growth. On the next day the washed sputa yielded practically a pure typhoid culture. The typhoid strains in both of these cultures gave positive tests for the typhoid bacillus in lactose litmus, litmus milk, plain broth, glucose agar, and from all cultures the active motile bacillus gave a strong positive Widal with a known typhoid-blood serum. The patient's blood serum gave a positive Widal in 1 to 40 dilution with a laboratory culture of the typhoid bacillus. On December 16 a culture made of the stools was negative of typhoid, but many colonies of *Bacillus coli* were found. During this period the spleen remained palpable. There was no tenderness of the abdomen, no tympanites of consequence, no roseolar eruption, and no diarrhea. The patient's mind remained clear, although she was ill and restless both day and night.

The patient continued very ill—weak, apathetic, much thirst, absent appetite, with continued fever ranging from 102.5 to 104° F. for the first four weeks, then a slightly remittent character ranging from 101 to 102° F. in the mornings to 103 to 104° F. in the evening until March, 1914. From March onward the temperature was frankly remittent and septic in type. The respirations ranged from 30 to 40 in the earlier stages of the disease, then diminished to 20 to 30 until the last two weeks of the patient's life, when the highest record was 36 per minute. The pulse was full, not very rapid, and of good quality for the first four weeks. After January 1 it rapidly increased and the quality became poor; the rhythm was regular. The blood-pressure gradually fell on December 24 to 105 systolic and 70 diastolic; on February 29 it fell to 90 systolic and 60 diastolic, where it remained until the end. The spleen continued palpable. No rose spots of the skin appeared at any time. The urine remained practically free of albumin, and contained only a few hyaline and hyalogramular casts at times. Cultures made from the urine revealed no typhoid bacilli at any time. Cultures of the stools made in the later stages revealed no typhoid bacilli. Additional

cultures of blood and sputa yielded typical growths of typhoid bacilli after three months in the hospital. Anemia gradually supervened, and on March 25 the red-blood cells numbered 3,650,000; hemoglobin, 55 per cent.; white-blood cells, 12,500; with small lymphocytes 7; large lymphocytes, 14; large mononuclears, 3; polymuclears, 76 per cent.

The consolidation of the whole right lung persisted; gradually softening occurred in the anterior upper lobe with all of the characteristic evidences of cavity formation. Moist bubbling rales and amphoric breathing were present over the upper lobe. Moist rales and bronchial breathing persisted in the lower right lung. The sputa became more abundant, contained elastic fibers, pus, and blood cells, typhoid bacilli, pneumococci, streptococci, and many indifferent bacteria. Numerous examinations failed to reveal the bacillus tuberculosis. During the last week hypostasis occurred in the left lower lobe. During the whole clinical course the mind remained practically clear. Although forced feeding was practised, emaciation was present. Death from exhaustion occurred on April 25, 1914, a little more than five months from the initial chill. An autopsy could not be obtained.

The patient's treatment in the early stages was that for pneumonia; after two weeks the treatment was that for typhoid fever. At one time 60 to 90 grains of urotropin were administered daily without any noticeable result. Supporting treatment, with strychnin by mouth or hypodermically and digitalis from time to time, was the chief drug therapy.

The notable events of this case history are as follows: The patient was seized suddenly with chill and fever and presented all of the physical phenomena one week later of a frank right lower-lobe pneumonia. A palpable enlarged spleen was found. Inasmuch as we have found an enlarged spleen in many of the Greek patients who are treated in the hospital for illnesses not usually associated with enlarged spleen, and on that account believed to be due to a malaria suffered in Greece, but little importance was placed upon this enlargement of the spleen. The leukocytosis of admission became less, with an increase of the consolidated area of the lung. On the seventeenth day in the hospital there was a positive typhoid-blood culture, and on the next day almost a pure typhoid growth was found in the sputa. The typhoid bacteremia and typhoid bacilli in the sputa persisted for more than three months, and were probably present at the time of death. The typhoid bacillus was not found at any time in the stools or in the urine.

Therefore this patient seems to present an example of typhoid fever presenting its primary manifestations in the lung in the form of a frank, outspoken croupous pneumonia.

MILD DIABETES IN CHILDREN.<sup>1</sup>

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THE fatality of diabetes in early life is an axiom that has come down to us through generations of text-books as a hoary tradition.<sup>2</sup> However, an increasing number of observations seems to show that juvenile diabetes need by no means be a mortal disease—that in childhood and youth, as in adult life, diabetes may run a favorable course.

URINE CHART.—CASE I

Date.	Quantity.	Reaction.	Specific gravity.	Albumin.	Sugar, per cent.	Remarks.
Dec. 24, 1910	....	Alkaline	1040	—	Considerable	Diacetic acid, 0.
Dec. 29, 1910	....	Acid	1027	—	Distinct	
Jan. 5, 1911	1500	Acid	1030	—	Distinct	
Jan. 12, 1911	2500	Acid	1025	—	—	
Jan. 14, 1911	2000	....	....	....	Trace	
Jan. 19, 1911	1750	Acid	1018	—	Trace	
Feb. 16, 1911	2375	....	1030	—	Trace	
June 10, 1911	....	Acid	1030	—	Trace	
July 13, 1911	....	Acid	1029	—	—	
Aug. 8, 1911	....	Acid	1019	Faint trace	Trace	Oxalates.
Dec. 11, 1911	2000	Acid +	1028	Trace	0.6	Urates; oxalates.
Dec. 27, 1911	....	Acid	1026	—	0.6	Oxalates.
Jan. 11, 1912	1650	Acid	1030	—	0.55	Oxalates.
May 18, 1912	....	Acid	1020	—	Trace	Diacetic acid, 0.
May 21, 1912	....	Acid	1031	—	Trace by fermentation	Diacetic acid, 0.
Nov. 8, 1913	....	Acid	1010	—	0.5	

CASE I.—For several years I have had under observation a boy and a girl—brother and sister—who when they first came to me gave me great concern. The boy, aged nineteen years, had been urged by his father to take out life insurance in order to learn lessons in economy. Though he believed himself perfectly well, he was rejected, naturally to his great consternation, because sugar was found in the urine. Before he came to me another physician had confirmed this fact and had given a gloomy prognosis. The boy had had no sickness of moment, except a mild attack of jaundice four years previously. I placed him on a carbohydrate-free diet,

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12, 1915.

<sup>2</sup> Since reading this paper, the statistics of De Lauge and Schippers (*Nederlandsch Tijdschrift voor Geneeskunde*, 1915, July 24, ii, No. 4, p. 637) have appeared. They found between 500 and 600 cases of diabetes in children recorded; recovery was mentioned in only 30 of the 500 cases, and these were not traced long. They themselves report 8 cases in detail. All terminated fatally, the duration varying from eight or nine months to two years and five months.



but the sugar persisted for a long time. There was usually a trace present at some time during the day, frequently in the morning specimen. The quantity of urine was not increased and there was no thirst. Indeed, aside from loss of weight, probably due to restriction in the food intake, the boy presented nothing abnormal, except a profound mental depression, for which a chance question gave me an explanation. I learned that a medical student had told him that diabetes in the young was absolutely hopeless. The sugar, tested by the reduction and the fermentation method, varied, as is shown in the chart, from traces to 0.6 per cent. Diacetic acid was never present. Without any other than dietetic treatment the boy finally lost his glycosuria, and no longer excretes sugar, though on a normal diet.

CASE II.—Shortly after the first case came under my observation, the boy's sister, aged seventeen years, presented herself on account of loss of flesh—in a few months her weight had dropped from 133 to 122½ pounds. She had thirst at times and a poor appetite. Menstruation was painful, but regular. Her color was pale—hemoglobin 70 per cent. The urine contained glucose from a trace to 0.7 per cent. The quantity varied from 1000 to 1500 c.c. in the twenty-

URINE CHART.—CASE II

Date.	Quantity.	Reaction.	Specific gravity.	Albumin.	Sugar, per cent.	Remarks.
Jan. 2, 1911	....	Acid +	1033	—	Trace ?	
Jan. 19, 1911	....	Acid	1040	—	Trace	
Jan. 23, 1911	1500	Acid	1030	—	Trace	
Jan. 30, 1911	1000	....	....	—	Distinct	
Mar. 7, 1911	....	Acid	1025	—	Trace	
Mar. 25, 1911	1250	Acid	1030	—	Trace	
May 27, 1911	1000	Acid +	1032	—	Trace	Diacetic acid, 0.
Oct. 22, 1911	....	Acid	1030	—	0.6	Diacetic acid, 0.
Oct. 29, 1911	....	Acid	1021	—	0.1	Diacetic acid, 0. Acetone, 0.
Feb. 3, 1912	....	Acid	1019	—	0.7	
April 3, 1912	....	Acid	1030	—	0.55	
May 26, 1912	....	Acid	1023	—	0.3	

four hours. (See Chart.) On a strict diet her weight fell to 110½ pounds, a reduction of 22½ pounds from her maximum weight. After ten months the weight began to increase, having reached when the patient was last seen 128¾ pounds. Coincident with this increase there was an improvement in her general condition, the hemoglobin rising to 84 per cent. The sugar has disappeared from the urine. A few months ago she was married and is living in the Middle West, enjoying the best of health.

CASE III.—The third patient is E. W., aged twenty-two years, the eldest brother of the two preceding. Aside from an attack of jaundice at thirteen, he had always been well. At any rate, though attending his family for many years, I scarcely knew him professionally until August, 1911, when he came because he was losing weight. Examination of the urine showed a trace of sugar.

He apparently recovered, for I did not see him again until November 6, 1913, when shortly after returning from his wedding trip he began to suffer from attacks of indigestion. His appetite was good, but he refrained from eating on account of the distress that followed. He had noticed that at the height of an attack he would pass a colorless urine. I again found a trace of sugar, although there was no polyuria, no thirst, no real diabetic symptoms. The digestive disturbances yielded promptly to treatment. I have not seen him for eighteen months, but know from his family that he is to all appearances perfectly well.

There is no diabetes in the parents of these patients nor in collateral relatives. A maternal aunt has gall-stones. The other five children (there are eight altogether) are, so far as I know—and at some time or another I have examined every one—free from glycosuria. The parents are exceedingly nervous, and the whole family, except the first patient, are very fond of sweets—so much so that the candy box is never closed.

CASE IV.—R. C., a girl, aged fourteen years, born in Russia, has a mother who has been diabetic for nine years. The child was well until three weeks before coming to the Polyclinic Hospital. At that time the mother noticed that she drank more water than usual, and passed urine oftener and in larger amounts, getting up from one to four times a night. She also had a little pruritus vulvæ, mostly on urination. Measles and a possible attack of whooping cough constitute all her previous illnesses. She has been a steady candy eater. Menstruation began at thirteen and has been regular and rather profuse, lasting eight days. The father and the other children—a brother and a sister—appear to be well. Physical examination of the child shows nothing abnormal. She weighs 88 pounds, which is a loss of 7 pounds since the beginning of her illness. The blood examination gave the following results: Red-blood cells, 4,850,000; hemoglobin, 88 per cent.; leukocytes, 12,600; polymorphonuclears, 61 per cent.; lymphocytes, 38 per cent.; eosinophiles, 1 per cent.; color index, 0.91.

In this patient the diabetic taint is more pronounced than in the others (see Chart, Case IV), yet under dietetic restriction she has not only become sugar-free, but has attained a tolerance of 90 grams of carbohydrate.

These four cases, particularly the first three, belong to an apparently well-defined group to which Frank<sup>3</sup> and Salomon<sup>4</sup> have called attention. Among Salomon's thirteen cases, however, only two are under the age of twenty-five. He employs the term *diabetes innocens im jugendlichen Alter*, although several cases over thirty-five years of age are cited in his list. The salient features of the mild forms of juvenile diabetes are:

<sup>3</sup> Die Therapie der Gegenwart, 1914, IV, 439.

<sup>4</sup> Deut. med. Wchnschr., January 29, 1914, p. 217.

1. The familial tendency—the existence of the disease in several members of the same generation.

2. The quantity of sugar tends to be low; in Salomon's analysis usually under 1 per cent., likewise, except in Case IV, in mine.

3. Salomon found that when 100 grams of glucose were added to the diet, only a small amount was eliminated in the urine, showing a high carbohydrate tolerance. In my fourth case, in which this test was tried, almost no sugar was recovered from the urine.

4. In many cases the blood sugar is about normal; in other words, there is no hyperglycemia.

DIABETIC CHART.—CASE IV

Date.	Quantity urine c.c.	Total calories per diem.	Grams dextrose in urine.	Grams dextrose in diet.	Weight.	Remarks.
Feb. 7, 1915	1200	1450	12	18	84 $\frac{1}{4}$	
Feb. 10, 1915	950	1500	11	18	85	
Feb. 11, 1915	900	1500	0	12	85	
Feb. 21, 1915	1175	1350	6	11	86 $\frac{1}{2}$	
Feb. 25, 1915	1500	1640	3	135	86 $\frac{1}{4}$	Oatmeal day.
Feb. 26, 1915	850	380	0	28	86 $\frac{1}{4}$	Green day.
Feb. 27, 1915	860	340	0	24		Green day.
Feb. 28, 1915	850	240	0	33	86	Green day.
Mar. 1, 1915	1400	340	0	29		Green day.
Mar. 2, 1915	900	1640	0	135		Oatmeal day.
Mar. 3, 1915	800	1440	0	12	84 $\frac{1}{2}$	
Mar. 17, 1915	1280	1450	0	12	86 $\frac{1}{4}$	
Mar. 21, 1915	1500	1700	0	72	88	
Mar. 24, 1915	1250	2000	0	128	89 $\frac{1}{4}$	
Second admission:						
April 29, 1915	750	1450	0	8	90 $\frac{1}{4}$	
May 1, 1915	1050	1720	0	38		
May 3, 1915	750	2000	0	68	90 $\frac{1}{2}$	
May 5, 1915	700	1980	Faint trace	94	91 $\frac{1}{2}$	100 grams dex- trose
May 6, 1915	650	1550	0	12		

The fourth case, the only one in which an estimation was made, showed 0.1 per cent. sugar in the blood on one occasion, and several weeks later 0.149 per cent.

Ketonuria may occur in these patients under a carbohydrate-free diet, but disappears rapidly when starches are given.

The first three of my cases fit very well into the category of so-called renal diabetes. The characteristics of this form, as established by Klemperer, Lépine, Frank, and Salomon, are as follows: The diabetes is mild; the daily output of sugar varies from a trace to 1.5 per cent., and is above this only when the amount of urine is small. The glycosuria is independent of the ordinary carbohydrate intake, and the ingestion of even large amounts of carbohydrate influences the glycosuria only to a slight degree—rarely are more than 20 grams per day excreted. Although the carbohydrate intake affects the sugar output but little within the limits given, it is possible to detect a slight increase under a rich carbohydrate diet and a decrease under a sparse or carbohydrate-free diet. Under a complete carbohydrate withdrawal

the urine may or may not become sugar free. The fact that in some instances it is impossible to render the patient sugar-free by a withdrawal of carbohydrate is, as Frank points out, not a sign of gravity, but is dependent upon the renal nature of the trouble.

CONCLUSIONS. 1. There exists a mild type of diabetes in childhood and adolescence.

2. The disease is peculiar in its tendency to occur in several members of the same family.

3. The glycosuria is usually moderate, although nervous excitement and other disturbing factors may augment it.

4. Other diabetic symptoms are often slight and may be wanting.

5. The disease is not progressive and may remain stationary or end in apparent recovery.

6. In its general features, it corresponds to the so-called renal diabetes.

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### FUNCTIONAL RENAL TESTS (PHENOLSULPHONEPHTHALEIN; LACTOSE) IN ORTHOSTATIC ALBUMINURIA.

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AND

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OUR knowledge of the subject of orthostatic albuminuria has recently been brought together and presented fully in an excellent article by Ludwig Jehle.<sup>1</sup> Jehle studied carefully, and analyzed, a large number of cases fulfilling the requirements of the condition as usually defined, namely, the excretion of albumin in the urine when the patient is in the erect position and the disappearance of albumin from the urine when the patient assumes the horizontal position. In addition to demonstrating, beyond question, the importance of the lordotic factor in the etiology of orthostatic albuminuria, and confirming the general opinion that the immediate cause is a renal circulatory disturbance resulting in a certain amount stasis, Jehle has also shown, in diuresis experiments, that this disturbance when operative leads to decrease in kidney function with oliguria and a low salt excretion; and, correspondingly, that when the disturbance is eliminated by the resumption of the horizontal posture, there is no impairment of kidney function as measured by the salt and water excretion.

<sup>1</sup> Die Albuminurie, *Ergeb. f. inn. Med. u. Kinderheilk.*, Leipzig, 1913, 808-912.

Jehle's study, while thorough as regards salt and water, did not include the application of two functional renal tests upon which a good deal of reliance is now placed, namely, the phenolsulphonephthalein test and the lactose test. We have had the opportunity to observe 6 cases of orthostatic albuminuria (4 of them patients in the private ward, and 2 in the public wards of the Johns Hopkins Hospital, 1 of the former cases is included, due to the kindness of Professor T. C. Janeway, to whose service the patient was admitted) in which the phenolsulphonephthalein test of Rowntree and Geraghty has been applied, and in one of them the lactose excretion was studied.

The individual cases are of interest in themselves, and may be briefly reported as follows:

CASE I.—H. W., white, male, aged sixteen years. Admitted February 3, 1914.

*Complaint.* Albuminuria.

*Family History.* Unimportant.

*Personal History.* Frequent tonsillitis until he had a tonsillectomy and adenoidectomy six years ago. Typhoid fever two years ago. For a year previous to this he outgrew his strength and was generally run down.

*Present Illness.* The patient was examined for life insurance one month ago, and albuminuria detected.

*Physical Examination.* Sparely nourished youth. Slight general glandular enlargement; definite increase in lumbar lordosis; lower pole of the right kidney palpable when the patient stands. Systolic blood-pressure, 125.

*Urine.* Urine voided while in the horizontal position was negative for albumin or casts, while that voided after standing erect for twenty minutes contained 18 grams of albumin to the liter, but no casts. Urine voided after standing erect for twenty minutes, with one thigh flexed, showed, still, 2 grams of albumin per liter.

Phenolsulphonephthalein excretion (patient recumbent):

First hour	62 per cent.
Second hour	7 "
Total	69 "

Phenolsulphonephthalein excretion (patient standing):

First hour	37 per cent.
Second hour	18 "
Total	55 "

*Roentgenogram of Right Kidney after Collargol Injection.* Right kidney slightly prolapsed, kinking of the ureter with slight hydronephrosis.

CASE II.—M. M., negro, male, aged sixteen years. Admitted February 4, 1914.

*Complaint.* Rupture.

*Family and Personal History.* Unimportant.

*Present Illness.* Four years ago a bulging appeared in the right groin. This is present when he stands and disappears when he lies down.

*Physical Examination.* Sparely nourished negro boy. Symmetrical decay of the upper lateral incisor teeth; slight tonsillar and general glandular enlargement; retromanubrial dulness; reducible left inguinal hernia; marked accentuation of the lumbar lordosis. Systolic blood-pressure varied between 118 and 100.

*Urine.* Numerous observations, with the patient recumbent, showed no albuminuria or cylindruria; while when the patient stood up the urine contained from 3 to 6 grams of albumin per liter and a few finely granular casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour . . . . .	64 per cent.
Second hour . . . . .	11 "
Total . . . . .	75 "

*Lactose Excretion.* The test was made in the usual way, by intravenous injection of 20 grams of milk sugar dissolved in 20 c.c. of distilled water, the solution having been previously Pasteurized at 75° to 80° for four hours on each of three successive days. The urine was collected at one to two hourly intervals and tested with Nylander's solution, and by the polariscope, until the reaction for sugar ceased to be positive. Normally, all the lactose is excreted in four to five hours.

The results in this case were as follows:

After one hour . . . . .	35.6 per cent.
Between one and two hours . . . . .	40.0 "
Between two and four hours . . . . .	11.2 "
Between four and six hours . . . . .	trace
Between six and eight hours . . . . .	none

CASE III.—W. E. S., white, male, aged sixteen years. Admitted June 16, 1911.

*Complaint.* "Kidney trouble."

*Family History.* Negative.

*Personal History.* Five years ago he had slight indigestion for one year.

*Present Illness.* The patient was examined four months before admission preparatory to entering West Point Military Academy and was told at that time that his urine was abnormal.

*Physical Examination.* Practically negative. Unfortunately, no data as to the degree of lumbar lordosis was made in the records. Systolic blood-pressure, 110.

*Urine.* The urine voided after remaining in bed contained no albumin, but on one occasion a few hyaline and granular casts were found. Two specimens of urine voided after the patient had been erect and walking about contained albumin and a few hyaline casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour . . . . .	42.7 per cent.
Second hour . . . . .	12.9 "
Total	55.6 "

CASE IV.—P. B., white, male, aged twenty-five years. Admitted May 2, 1914.

*Complaint.* "Stomach trouble."

*Family History.* Grandfather died of tuberculosis.

*Personal History.* Practically negative.

*Present Illness.* Began four years ago with a feeling of general weakness. Eight months ago he noticed dull pain in both legs and paresthesias of the face and scalp. He suffered from an acute gastro-intestinal upset six months ago, and since then has had occasional nausea and abdominal pain after meals.

*Physical Examination.* A little pallor of the mucous membranes; slight general glandular enlargement and arterial thickening; marked increase in the lordosis of the lumbar spine. Systolic blood-pressure varied between 125 and 120.

*Urine.* When the patient was recumbent, the urine voided was free from casts or albumin, but urine voided on standing showed, on testing, a definite cloud of albumin but no casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour . . . . .	54 per cent.
Second hour . . . . .	18 "
Total . . . . .	72 "

CASE V.—T. D. W., white, male, aged twenty-four years. Admitted December 12, 1914.

*Complaint.* Chronic constipation, albuminuria.

*Family History.* Unimportant.

*Personal History.* Scarlet fever in addition to the usual diseases of childhood. Malaria at six. Chronic constipation for six years, initiated by irregularity in going to stool and dependence on cathartics.

*Present Illness.* Gradual onset one year ago. The patient found himself growing lazy and spiritless. Three months ago his physician discovered a trace of albumin in his urine.

*Physical Examination.* Practically negative, save for a moderate accentuation of lumbar lordosis.

*Urine.* While the patient was in bed the urine contained no albumin or casts; when standing erect a trace of albumin appeared

as well as a few hyaline casts. A specimen voided after he had stood for some time in an exaggerated lordotic position contained 2 grams of albumin per liter, but no more casts were found.

Phenolsulphonephthalein excretion (patient recumbent):

First hour . . . . .	51 per cent.
Second hour . . . . .	20 "
	—
Total . . . . .	71 "

CASE VI.—J. A., white, male, aged seventeen years. Admitted to the service of Professor Theodore C. Janeway April 17, 1915.

*Complaint.* Albumin in the urine.

*Family History.* Unimportant.

*Personal History.* He had the usual exanthemata and frequent tonsillitis as a child. An adenoidectomy was done four years ago. Malarial fever during two successive summers, four and five years ago.

*Present Illness.* On applying for life insurance six months ago, albumin was detected in the urine. Of four subsequent urine examinations, two showed albuminuria, one cylindruria, and two were entirely negative.

*Physical Examination.* Well-nourished youth. Moderate increase in the lower lumbar lordosis, otherwise practically negative. Systolic blood-pressure, 120.

*Urine.* The urine voided in the morning after a night in bed was entirely negative for albumin or casts. Exaggeration of the lumbar lordosis, while the patient was in bed, brought out a marked cloud of albumin, but no casts.

On two occasions, after standing in an exaggerated lordotic position for one-half hour to an hour, there was, in spite of a large water-intake, a definite oliguria, and the urine contained 6 grams of albumin to the liter as well as a good many granular casts. After this procedure, although the patient was put back to bed, the urine voided throughout the remainder of the day still contained a trace of albumin, but no more casts were found.

Phenolsulphonephthalein test (patient recumbent):

First hour . . . . .	46 per cent.
Second hour . . . . .	18 "
	—
Total . . . . .	64 "

Phenolsulphonephthalein test (patient standing):

First hour (first fifteen minutes in exaggerated lordosis)	52 per cent.
Second hour (up and strolling about)	12 "
	—
Total . . . . .	64 "



In the above 6 cases the phenolsulphonephthalein test showed that the excretion of this substance was entirely normal, save in two instances. In one, the case of W. E. S., it was 5 per cent. lower than the usually accepted normal. In the other, the case of H. W., it was 14 per cent. lower with the patient standing, than when made in the recumbent position. The latter observation is in accord with Jehle's studies of the salt and water excretion. However, in the case of J. A., it is to be noted that there was no reduction in the amount of the dye recovered in the urine, even when the conditions producing oliguria and the maximum degree of albuminuria were present.

The observation of a larger number of cases will be necessary before definite conclusions can be drawn in regard to this point. Unfortunately, a comparison of the excretion in the recumbent and in the erect posture was not made in the other four patients.

In this connection we may mention the case of a young man sent for study because of supposed renal disease. Our examination of the urine revealed no abnormalities either in the recumbent or in the erect position. The lumbar lordosis was a little exaggerated, however, and on making the patient stand in a purposely exaggerated lordotic position for one-half hour he excreted a trace of albumin and a few hyaline casts. The phenolsulphonephthalein test was made with the patient recumbent, and again in the ordinary erect posture. The amount excreted in the recumbent position was for the first hour, 58 per cent.; for the second hour, 20 per cent.; total, 78 per cent.; while that put out while standing erect was for the first hour, 57 per cent.; for the second hour, 13 per cent.; total, 70 per cent. We do not regard a difference of 8 per cent. of great significance, especially when the readings are high, as in this case.

We should like to call attention, in the instance of H. W., to the fact that a collargol Roentgen-ray plate of the right kidney showed a definite prolapse, with kinking of the ureter, and some hydronephrosis; and we would suggest that, in certain instances, at least, a movable, or a prolapsible, kidney may be a factor in so-called orthostatic albuminuria.

## THE EFFECT OF WATER INTAKE ON NITROGEN RETENTION IN NEPHRITIS.

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THE notable fact which has been established by study of the metabolism of patients with nephritis, is that there are periods

when organic and inorganic substances are retained in the body to a degree not evident in health. Whether this accumulation be dependent upon an inability of the kidney to excrete these substances, as some believe, or whether these substances are retained in the tissues bound in some abnormal combination, is not at present clear. The net result, however, is the same in that balances between intake and output are either difficult to achieve, or at periods quite impossible. In the nature of the factors operating to effect this retention, we come to one of the fundamental questions in pathological metabolism, concerning which our conceptions are vague and, for the most part, devoid of support. The relation of sodium chloride to edema may be cited as an example. Is the salt retained in the tissues, or is there a failure of the kidney to excrete? Is it the sodium or the chlorin that is the immediate factor, or is the whole question one of water retention with the salt as a passive factor? From facts so equivocal, evidently nothing can be derived that may serve as a principle for rational therapy.

It is, however, evident that even though we are able to achieve the ultimate refinement of accuracy in diagnosis of a renal lesion, treatment must depend very largely on our knowledge of the metabolism which usually accompanies this special clinical picture. Various tests may tell us something of the severity of the lesion, but nothing as to what measures are required to meet the impaired functional ability of the kidney, nor how to facilitate the irreducible minimum of its work.

These studies of the metabolism of patients with nephritis were carried on primarily in the hope of disclosing some facts which might be of help in the treatment of these cases. Years of observation, I must admit, have added only to my feeling of uncertainty and skepticism regarding the procedures commonly used, and in the absence of a single rational principle there seems no guide. It was the plan in this study to take certain definite conditions of diet, etc., as a basis, and to observe effects of alterations of single factors. Since it was desirable to continue observations over considerable periods, the diets often used in metabolism studies could not be employed because the patients too quickly tire of them. For this reason we used the ingredients of an ordinary mixed diet, only preserving some factors, *e. g.*, nitrogen, at a minimum. Complete analyses were made of these diets. At once we meet an obstacle in the comparison of the protein metabolism of a normal man with that of a sick patient. The latter may have difficulty in eating a certain small ration which is quite inadequate for the man in health. Our controls are, on this account, not of so much service as in other studies where the patient is not so sick. They serve simply as a background of the normal response to a definite dietary regimen. As the fuel values of these diets hardly exceeds 1300 calories, it follows that the patient is usually insuffi-

ciently nourished; but it often happens that an adequate amount of food can not be ingested and retained by patients with nephritis at those periods of the disease where these investigations are most instructive. A consideration of the metabolism of undernutrition shows that no source of serious error of interpretation is introduced into the investigation by these conditions. If the food intake be below the immediate requirements of the organism for energy the deficit is made good at the expense of body fat (and stored glycogen). This loss becomes manifested in a fall in body weight. There is even in starvation a marked conservation of protein in the organism, and under conditions of slight undernutrition the protein destruction for energy or heat is extremely slight. Toxic protein destruction is another matter, and need not be considered when the temperature range is normal.

The second feature relative to the diets employed concerns the amount of nitrogen which was purposely reduced to a very low amount. The normal person is constantly tending to a condition of nitrogenous equilibrium between intake and excretion, and if protein food be much reduced there is a gradual fall in nitrogen excretion, until after a few days a balance is struck.

Nitrogen is retained to the body normally under two conditions only: during growth, when muscle tissue is being built up, and during convalescence, after periods of disease that have caused tissue destruction; both conditions demarked by gain in weight. Sharply contrasted with these normal states is the phenomenon peculiar to some types of nephritis wherein for periods of time the nitrogen excreted is considerably less than the intake, and there is, synchronously, a loss in, or stationary, body weight unless edema develops. These generally accepted facts which contrast the nitrogenous metabolism of some types of nephritis with the normal are briefly outlined as a basis for our further consideration.

**METHODS.** The methods of study of metabolism in animals have been adopted, so far as possible, in this work. The ingredients of each diet were weighed before each meal, and particular care was exercised to see that all the food given to a patient was eaten. Like portions of food were taken from the ward pantry for analyses. The preparation of the food was intrusted to a competent nurse who understood and realized her duties. Urine was collected from 6 A.M. to 6 A.M., and at the latter time the patient was required to empty his bladder. The urine specimens were analyzed separately; the feces in periods. Unless specifically noted in the charts the nitrogen of the feces is deducted from the total nitrogen intake for the period.

**NITROGEN RETENTION WITHOUT EDEMA.** From the study of metabolism in a series of cases of renal disease, it is observed that departures from the normal are noted chiefly in respect to nitrogen or sodium chloride. While with some cases the abnor-

mality affects only nitrogen with others, salt is also retained as well as nitrogen. The remarkable degree of nitrogen retention evidenced in some cases is not generally appreciated, and the pertinent question here arises, What becomes of this retained nitrogen? As an example of one of the questions at issue, the following case is cited when there was a retention of three grams of nitrogen per day.

CASE I.—W. H., aged forty-eight years. Admitted December 17, 1913, complaining of headaches and swelling of the face and ankles.

Excepting pneumonia in 1899, he had had no serious sickness. The present illness began about eighteen months before admission, with dyspnea on exertion. For six months there has been vomiting almost daily, sometimes two or three times a day. There was no gastric distress other than nausea. During this period severe headaches have been frequent, and there have been puffiness of the eyes and swelling of the feet. There have been no visual disturbances. The appetite has been good; bowels regular.

*Examination.* The patient is poorly nourished, with slight edema of the face. Retinæ hazy, but no exudate or hemorrhages. Moderate cardiac hypertrophy. Systolic retraction in fifth, sixth and seventh spaces outside the nipple; no evidence of valvular disease. Pulse is small and of low tension; blood-pressure, 134 mm. Hg. Liver enlarged, 10 cm. below costal margin in the right midclavicular line; smooth and not pulsating. Slight edema of legs and feet. Blood: hemoglobin, 80 per cent.; leukocytes, 10,000. Wassermann, negative. Urine: 1500 c.c.; specific gravity, 1009; albumin, +; casts, ++; leukocytes, +; phenolsulphone-phthalein test, 28 per cent.

The edema subsided quickly and the liver became perceptibly smaller during the first week. The patient was apparently doing very well.

TABLE I.—METABOLIC STUDY OF PATIENT W. H.

Date, December,	Amount urine, c.c.	Nitrogen + albumin, gms.	Nitrogen, gms.	NaCl, gms.	Sulphur, gms.	Phos- phorus, gms.	Weight, pounds.
19	1780	5.26	4.34	4.27	0.46	0.56	97½
20	1570	4.19	3.83	3.30	0.41	0.38	96
21	1420	...	3.47	4.12	0.29	0.33	95
22	1550	...	4.14	5.43	0.36	0.30	92½
23	860	3.22	2.98	3.61	0.33	0.27	92
24	1560	5.40	3.95	7.02	0.41	0.34	87½
			22.71	27.75	2.26		
		Ingest	41.75	45.21			

Balance . . . . . +19.04    -12.54  
Fluid intake 500 c.c. daily.

N : S = 10 : 1

On December 23 there was noted a weakness of the right hand, and the next day the patient showed distinct weakness of all muscles of the right half of the body, including those of the face. There was no change in sensation or of the reflexes. There was no disturbance of consciousness; no headache; no other prominent symptom. The patient felt well, except that he was naturally worried about his paralyses. All of these central symptoms cleared up during the next ten days, so that no residual of the paralyses was detectable.

The marked retention of nitrogen, increased until the climax, was of special interest with this history and in relation with the blood-pressure chart.

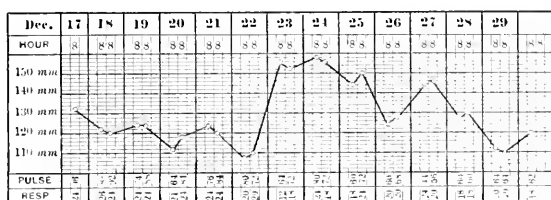


CHART I. Blood-pressure chart. W. H.

Several interesting considerations arise from the metabolic study. The edema which was evident on admission to the hospital subsided rapidly, and explains in part the rapid loss in weight. If this loss were all water it represents nearly five liters, which might seem improbable in view of the moderate edema detectable. There is, however, a difference of over five liters between the fluid ingested and the volume of urine excreted. This fact brings into prominence the lack of concord between the sodium chloride loss and water loss from that necessary for isotonic solutions in the body.

The salient features presented in the study of this case are: a normal water elimination and an apparent washing out of sodium chloride—negative balance—but at the same time marked retention of nitrogen with a climax synchronous with the development of a transient paralysis. The condition of affairs clearly parallels the uremic symptoms which von Leube cautioned are likely to follow the sudden subsidence of edema after diaphoresis. One is led to imagine here a loss of water only, and in consequence of this an increase in concentration of some excretory materials in the blood and tissues.<sup>1</sup> The highest concentration of nitrogen in the

<sup>1</sup> E. E. Butterfield has investigated a series of blood sera, using purely physico-chemical methods. The results are interesting and very significant. The physical changes in the sera of various types of nephritis mirror the more obscure chemical deviations from normal. Thus in the type of case under discussion the slight increase in specific gravity, dry residue, and refraction index means concentration, while the freezing-point indicates a disproportionate increase in some other ingredients.

urine is a little better than 0.2 per cent., and one is led at once to conjecture regarding the total nitrogen elimination had the urine volume been doubled. In other words, is the nitrogen excretion in any degree a function of the urine volume? This case is given, perhaps, unnecessary discussion, since it is in some essential particulars typical of a number that have been studied. It illustrates, as they all do, a relation that appears to obtain quite constantly between marked nitrogen retention and some of the terminal sequelæ of severe nephritis. When there is a rapid accumulation of nitrogen in the body under these circumstances, either uremia, apoplexy, or cardiac failure seems predictable.

It has been accepted that one of the characteristic phenomena of the type of nephritis under discussion is that the nitrogen concentration of the urine is low. While a normal urine may contain 2 or even 3 per cent. of nitrogen, with this form of nephritis the "kidney is not able to concentrate," and a liter of urine may contain even less than ten grams of nitrogen. Concentrations of much below 1 per cent. even when the fluid ingest is restricted are not of unusual occurrence. It would seem, then, from this that the completeness of elimination of excretory nitrogen is dependent upon the amount of diluting medium, other factors being equal; in other words, if the nitrogen to be eliminated is 12 grams, and the maximum concentration effected by the kidney 0.5 per cent., the necessary urine volume must equal 2400 c.c. We have made a number of observations which appear to support this conception.<sup>2</sup> With the following case, which is typical, the evidence recorded in the chart shows that a plus or minus nitrogen balance is dependent on the urine volume, that is, the fluid ingested. In all other respects the periods are exact duplicates.

CASE II.—H. K., aged forty years.

*Past History.* Patient had scarlet fever at five years of age and pneumonia when twenty-two. Has never been robust, but has been well. No history of nycturia or edema until two months ago. Venereal diseases denied.

*Present illness* began seven weeks before admission, with headaches, mostly occipital, but involving vertex and frontal regions at times. More recently there has been some shortness of breath, and the patient has grown weaker. At this time there was swelling of the face about the eyes and later some swelling of the ankles. The patient has noted that for the past month he has had thirst at night and passed much urine. There have been cramps in the legs.

This is further emphasized in differences between total dry residue and the protein under various conditions: Normal dry residue minus protein, 1.8; nephritis with edema, dry residue minus protein, 2.2; nephritis with uremia, dry residue minus protein, 3.3.

<sup>2</sup> We have studied 22 cases of nitrogen retention, and these reported represent fair examples.

TABLE II.—METABOLIC STUDY OF PATIENT H. K.

Date, April.	Amount urine, c.c.	NaCl, gms.	Nitrogen, gms.	Weight, pounds.	
9	900	2.88	5.06	119	Metabolic diet.
10	880	2.90	4.85		
11	1920	5.95	9.62		Fluids, 800 c.c.
12	1430	4.72	6.68	117 <sup>1</sup>	
<hr/>					
				26.21	
				28.86 (ingest)	
				<hr/>	
				+2.65 (balance)	
13	2090	6.69	9.64		
14	2190	7.88	11.29	117	Force fluids.
15	1940	6.01	9.31	116 <sup>1</sup>	
16	2220	6.16	9.56		
<hr/>					
				39.80	
				29.53 (ingest)	
				<hr/>	
				-10.27 (balance)	
17	1580	4.27	7.49	114	Milk, 1200 c.c.; water, 800 c.c.
18	1500	3.45	6.86	113	
19	1840	3.49	8.93	112 <sup>1</sup>	
20	1540	3.23	6.87	111	
21	1760	2.29	8.25	111	
<hr/>					
				38.40	
				27.22 (ingest)	
				<hr/>	
				-11.18 (balance)	
22	1100	1.43	5.47	111	Metabolic diet + fluids.
23	1030	1.24	5.30		500 c.c.
24	750	2.63	4.50		
25	850	1.02	5.34	111	
26	820	1.48	4.92		
27	910	1.55	5.93	112	
28	1180	2.60	6.68		
<hr/>					
				38.14	
				51.10 (ingest)	
				<hr/>	
				+12.96 (balance)	
29	1360	3.12	7.43	112 <sup>1</sup>	
30	1470	3.09	8.57		Force fluids.
<hr/>					
May					
1	1480	3.26	6.02	113	
2	1330	2.79	7.75		
3	2290	4.12	11.12	114 <sup>1</sup>	
4	2160	4.01	9.01		
5	2100	4.20	9.60	117	
6	1490	3.13	8.09		
7	1400	2.94	7.81	118	
8	1560	2.72	8.26		
9	1760	2.99	8.55	120	
10	1840	3.50	8.41	119 <sup>1</sup>	
<hr/>					
				100.65	
				89.57 (ingest)	
				<hr/>	
				-11.08 (balance)	

*Examination.* The patient was a rather poorly nourished man, and looked anemic. The examinations disclosed a moderate degree of cardiac hypertrophy and some edema of the legs. Blood: hemoglobin, 54 per cent., otherwise of no significance. Wassermann reaction negative. Blood-pressure, 178 mm. Hg. systolic. Urine: twenty-four-hour quantity, 1600 c.c.; specific gravity, 1012; albumin, ++; hyaline and granular casts and leukocytes. Phenol-sulphonephthalein test; 5 per cent. recovered in two hours. After four days of observation the patient was given the measured diet. An initial diuresis on April 13 was due in part to edema fluid. On the next three days the patient was encouraged to drink water freely. The rise in nitrogen excretion is striking.

In the first period (April 9 to 12) there is a retention of two grams of nitrogen, a minus chloride balance, and a falling weight curve. The loss in weight continues until April 21, when the chloride balance is struck between intake and output. In the second period, April 13 to 16, there is a sharp increase in nitrogen excretion, so that in four days ten grams more nitrogen are excreted than ingested. As the patient began to tire of the diet a change was made to milk from April 17 to 21, involving a slight drop in the nitrogen intake. During this period the patient was urged to take water enough to make the total fluid ingested up to two liters. Here, again, the balance for the period shows a nitrogen loss to the body of eleven grams. The patient's condition had now become excellent, and he was kept in bed only to assure of accuracy in the study.

Thus far the nitrogen excretion has appeared to bear some relation to the volume of the urine. Is this the case actually? If it be so then a restriction of the fluid ingested should be accompanied by a retention of nitrogen in the body, *i. e.*, a plus-nitrogen balance. The fluid ingested was limited to 500 c.c. daily in the period April 22 to 28 and the metabolic diet was resumed. All other conditions were the same as in the earlier periods except that the patient was in much better condition. It is to be observed that the drop in the urine volume consequent upon limited fluid intake is at once followed by a fall in the nitrogen output. On no day did the urinary nitrogen equal the nitrogen of the food, and the period shows a retention of nearly thirteen grams. There was also a rise in the non-protein nitrogen of the blood at the end of the period. There is, then, in this case, an intimate relation between the nitrogen balance and the water excretion.

The increase of fluids in the next period points again to a washing out of retained nitrogen and a negative balance for the period.

One might be inclined to attribute the retention in the period April 22 to 28 to tissue regeneration, because there was a gain of a pound in weight; but this interpretation is negated by the continued gain in the following period, April 29 to May 10, when there was constant nitrogen loss.



A fact in relation to the chloride excretion deserves attention, since it is frequently noted in our studies. From April 9 to 21 the tendency is toward chloride equilibrium, with a more prompt excretion accompanying the periods when the urine volume is large. On April 21 the excretion is the same as the intake. During the next period there is a retention of a slight amount, followed by a negative balance in the final period.

This patient left the hospital in excellent condition and free from symptoms.

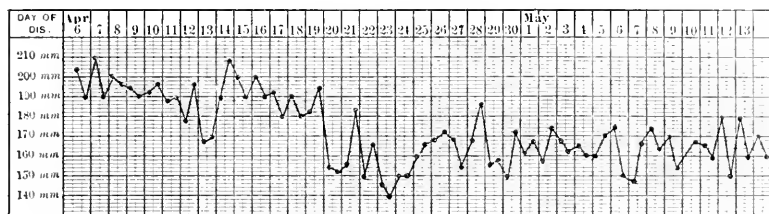


CHART II. Blood-pressure chart. H. K.

The relation between the urine volume and the nitrogen excretion appears with considerable constancy in this type of chronic nephritis. This case given in detail is not exceptional, but rather typical.

The following case presents the same essential factors as the last:

CASE III.—R. B., aged thirty-eight years.

*Past History.* Patient had scarlet fever in childhood and has had attacks of tonsillitis during his life. Patient was operated upon for appendicitis in 1903. At this time albumin was found in the urine. Has had no symptoms of renal disease until 1914. The patient contracted lues in 1896, and was treated. Several years ago he was treated again with salvarsan.

*Present History.* For three months there has been increasing dyspnea, especially at night. There has been some cough. He has lost in weight and his appetite is poor. Urine is passed freely, two or three times during the night. There has been very little headache, no visual disturbances, and no notable edema.

*Examination.* This disclosed slight cardiac hypertrophy, with a blood-pressure of 158 mm. Hg.; no edema; no retinal changes; hemoglobin, 78 per cent.; Wassermann doubtful. The urine amounted to 1075 c.c. for the first day. Specific gravity, 1013; albumin, heavy trace; a few hyaline casts. Phenolsulphonephthalein test, 7 per cent. The non-protein nitrogen of the blood was 88 mg. per cent.

This patient left the hospital much improved, although it was evident that the prognosis was definitely bad. The phenolsulphonephthalein test was never better than 10 per cent. for two hours. In a study conducted on this patient four months later it was found that his kidneys were unable to excrete more than eight grams of

nitrogen per day under any conditions. If the water ingested was adequate to secure a urine volume of 2400 c.c. or over, the nitrogen ran from seven to eight grams, irrespective of how large the protein intake might have been. If, on the other hand, the urine volume were low, the total nitrogen would be low.

TABLE III.—METABOLIC STUDY OF PATIENT R. B.

Date, March.	Amount urine, c.c.	NaCl, gms.	Nitrogen, gms.	Weight, pounds.	
16	1620	6.48	6.77	127	Metabolic diet, + 500 c.c. water.
17	1470	5.29	6.80	.....	Non-protein N, 88 mg.
18	1400	4.90	7.66	124	
19	1390	4.45	7.53	123½	
20	800	2.40	4.25	123½	
				32.99	
				36.44 (ingest)	
				+3.45 (balance)	
22	1730	4.00	8.58	124	Increased water intake.
23	1950	3.40	7.56	125	
24	1900	4.20	8.58		
25	1400	3.45	7.54	124½	
26	1840	3.20	7.79	124	
27	1720	3.24	8.43	125	
28	2220	3.45	9.48	125½	
29	1520	1.92	5.16	125	
				63.12	
				50.75 (ingest)	
				-12.37 (balance)	

CASE IV.—D., aged forty years, tailor.

*Family History.* Father and mother died of old age.

*Past History.* Malaria in childhood. Has never been sick until the present trouble commenced, six months ago. Alcohol in moderation. Venereal infection denied.

*Present Illness.* This began six months ago, with headaches in the morning. The headaches were frontal at these times. The patient noted that the breath was foul. The headaches have increased in frequency and the patient has been attending Cornell Dispensary for relief. The eyes have been swollen at times, but not the ankles. He has had frequent urination for two weeks. No dyspnea.

*Examination.* Well-developed man; looks anemic; face somewhat puffy. Pupils react normally. Albuminuric retinitis on both sides. Thyroid normal. Lungs normal. Vascular: pulse equal, regular, of good force, tension increased; artery, sclerotic. Blood-pressure, 180 mm. Hg., systolic. Heart: precordial impulse heaving and not localized. Relative dullness from right sternal margin to 12 cm. to left in fifth, intercostal space. No murmurs. Aortic

second accented. Abdomen: normal. Liver and spleen: normal. Extremities: no edema; reflexes normal. Glands not enlarged except those in cervical region, which are palpable. Weight: 119.5 pounds. Blood: hemoglobin, 70 per cent. Erythrocytes, 5,000,000. White-blood cells, 18,000. Wassermann negative. Non-protein nitrogen, 132 mg. Urine: 1010 c.c.; specific gravity, 1012; albumin, very heavy precipitate. Many hyaline and granular casts; a few white-blood cells; no red cells. Phenolsulphonaphthalein test on March 24, 11 per cent. recovered and a lactose test on the 25th showed no excretion up to fourteen hours. Phthalein test, April 7, 16.7 per cent. in two hours; and on May 5, after discharge, he returned to the hospital for the test, which was 14 per cent. The systolic pressure was irregular from day to day, with limits of 210 and 170 mm. Hg.

As this patient appeared very sick at the time of admission the metabolic diet was not used, but instead milk, in measured amounts, supplemented by arrow-root to increase the caloric value. The metabolic diet was commenced on April 15.

TABLE IV.—METABOLIC STUDY OF PATIENT D.

Date, March.	Amount urine, c.c.	Total nitrogen.	NaCl, gms.	Sulphur, gms.	Phosphorus, gms.	Weight, pounds.	
26	850	7.10	0.51	0.51	0.50	...	Non-protein N, 130
27	1160	10.47	2.90	0.65	0.68	116	mg.
28	1100	8.88	1.65	0.41	0.54		
29	1150	8.70	2.53	0.51	0.54		
30	1490	12.19	3.58	0.67	0.68		
31	1070	7.74	2.14	0.39	0.42	116	
		55.08	13.31	3.17			
	Ingest	45.17	15.66				
		-9.91	+2.35	balance			
April.							
18	2070	7.92	5.38	0.63	0.54	114	Force fluids.
19	2360	9.52	6.37	0.74	0.63		
20	1730	6.64	3.80	0.50	0.46		Non-protein N, 15
21	2910	11.00	8.15	0.82	0.73	116	mg.
		35.08					
	Ingest	29.26					
		-5.82	balance				

NaCl and nitrogen of feces subtracted from ingest.

With Case IV there was a negative nitrogen balance attained with relative ease when the protein of the diet was reduced. The flushing out of nitrogen was accompanied by a fall in the non-protein nitrogen of the blood to nearly a normal concentration. The weight remained almost constant. In the second period the fluctuation of the chloride excretion with the urine volume was notable; a phenomenon already mentioned. Chloride metabolism

was not normal, although compensation is attained in an irregular manner; there was no evident edema.

This patient was discharged much improved and sufficiently well to be able to secure life insurance, as he confided to a house officer at the time of a "follow-up" call.

These cases are illustrations of more or less successful application of a principle to attain a definite result: the prevention of nitrogen retention and the washing out of nitrogen retained during some previous period. As a method in practice one must make every reservation as to its efficacy. The cases that are found in hospital wards are, for the most part, representative of advanced stages of the disease where but little benefit at best can be expected. We do not at present know whether periods of nitrogen retention accompany the earlier and often transitory manifestations of renal disease. It is possible only to cite the facts that when this faulty elimination persists for some period and is of a marked degree there ensues some of the phenomena characteristic of uremia. I do not believe we are even able to assert that the latter state is a consequence of retention and not merely an associated phenomenon.

Now it is self-evident that large amounts of fluid can not be taken by every nephritic without danger. Each liter of water ingested represents an appreciable extra burden thrown upon the heart muscle, and with nephritis of all types we find this muscle abnormal and especially so with these cases of nitrogen retention. Hence it follows that with every case caution is necessary, and with some the procedure might be, theoretically, hazardous. A slowly developing water retention has been noted in some cases without evidence of cardiac embarrassment, yet we have held this water retention to be of cardiac origin, and are supported in this belief by the fact that digitalis often causes a prompt elimination of the surplus.

With cases where the renal damage is so extensive that there is no margin of accommodation or where water elimination is impaired no result is secured by forcing of fluids.

The following case is of the latter type:

CASE V.—T. C., aged thirty-eight years.

*Past History.* Patient has never been confined to bed until the onset of his present illness. He has had slight rheumatic pains at times, but not of such severity as to require medical attention. In habits the patient is moderate; he has used a little beer occasionally, but very seldom whisky. He has had gonorrhea, but never lues so far as he knows, and gives no history suggesting infection. His normal weight is about 110 pounds. r

*Present Illness.* Patient has had headaches for a week; prior to this symptom he believed himself in good health. Three days ago he noted that his face and eyes seemed puffy, but there was

no swelling elsewhere. The urine has been scanty for several days. The color was not noted. He has had no visual disturbances; no dyspnea or nausea.

*Examination.* Edema of face, especially about eyes. Moderate anemia; pyorrhea alveolaris; cardiac hypertrophy, with a faint diastolic murmur at the left sternal margin and a short systolic murmur at the apex. Pulse not Corrigan type. Lungs seem normal; abdomen normal. Slight pretibial edema; no glandular enlargement. Blood: hemoglobin, 65 per cent.; leukocytes, 6900. Wassermann negative (three tests). Blood-pressure, 160 to 130. Non-protein N, 180 mg. Urine: 800 to 1000 c.c.; specific gravity, 1014; albumin ++; casts and a few erythrocytes. Phenolsulphonephthalein test, 10 per cent. in two hours.

The patient was given the metabolic nephritic diet, beginning April 1. On April 13 this diet was changed to one of milk and arrow-root starch. The patient left the hospital improved so far as concerned symptoms. The headaches ceased and edema subsided. There was no change in the albuminuria. Two weeks after discharge he was readmitted with moderate edema, which disappeared promptly with the use of theocin. There was pronounced diuresis and a fall in weight from 112 pounds to 103 pounds.

TABLE V.—METABOLIC STUDY OF PATIENT T. C.

Date, April.	Amount urine, c.c.	Nitro- gen, gms.	N+ albu- min, gms.	NaCl, gms.	Sul- phur, gms.	Phos- phorus, gms.	Weight, pounds.	
5	1080	7.08	8.25	4.75	0.44	0.29	110	800 c.c.
6	990	5.89	7.53	3.86	0.35	0.23		water.
7	1040	7.00	8.77	3.95	0.43	0.29		
8	770	4.74	6.54	2.62	0.32	0.15	111	
9	950	7.74	8.61	5.23	0.53	0.39		
10	680	4.46	5.74	2.04	0.34	0.12		
11	840	5.17	6.99	2.52	0.42	0.19		2800 c.c.
12	900	5.49	7.08	2.70	0.37	0.22	112	fluid
		47.57	59.51	27.67				
	Ingest	58.12		20.88				
	Balance	+10.55		-6.79			N : S	14 : 1
13	790	4.64	6.12	2.29	0.31	0.17	112	1200 c.c.
14	820	4.77	6.31	2.39	0.32	0.19		milk; 50
15	810	6.60	7.85	2.89	0.43	0.30	113	gms.
16	800	5.18	6.43	2.00	0.29	0.27		starch.
17	850	4.89	6.20	2.72	0.27	0.28	111	
		26.08		12.29				
	Ingest	28.75		10.41				
	Balance	+2.67		-1.88			N : S	= 16 : 1

The patient returned to his home but did not attempt to work. Headaches returned in the latter part of May, and there was

dyspnea and some nausea. Edema did not appear. On June 2 the patient's wife noted twitching movements of the hands and face which alarmed her, and hospital aid was requested. The patient had an epileptiform convulsion in the ambulance and was admitted to the ward in coma. Death occurred the day of admission. No autopsy. Clinical diagnosis: chronic nephritis; chronic valvular disease (aortic insufficiency); uremia.

The table in this case shows a low urine volume, with no visible response to increase in fluid ingest; a small negative chloride balance and a marked tendency to retain nitrogen. The high non-protein nitrogen at the beginning of the study indicated that successful therapeutic measures would be marked by a negative nitrogen balance. This could not be secured. In the second period, with even further reduction in the nitrogen ingest, there still persisted a plus balance and the non-protein nitrogen practically unchanged. Here it was evident at the time of the first admission to the hospital that the rapid improvement in the patient's condition could not be continued nor were his kidneys adequate to any larger demands than those of a highly restricted diet. The discussion of cases such as this represents, naturally focusses upon the nitrogen exchange, but the morbid state is hardly more evident with the nitrogen than with other elements concerned in protein metabolism; both sulphur and phosphorus excretion are below what they should be and there are no compensatory days. With these facts in view the terminal event is entirely logical and was expected.

Everyone who has studied the metabolism of cases of nephritis has observed a retention of amounts of nitrogen in excess of what can be explained by increases of the non-protein nitrogen of the blood. A retention of a gram a day is common, two or three grams a day for a couple of weeks not rare. What becomes of fifteen or twenty grams of nitrogen so retained by a patient whose condition excludes the idea of cellular growth? Not half this amount of nitrogen can be accounted for in the blood on the basis of the degrees of the non-protein nitrogen observed.<sup>3</sup> It is evident that the surplus must be in the tissues, either free or combined.

In an attempt to gain some light on this point a series of analyses has been carried out on various tissues from cases of nephritis in comparison with other diseases, and it is apparent that the non-protein nitrogen in tissues accumulates to a remarkable degree. This is true of muscle (psoas) and of liver tissue, whether of all we are not as yet prepared to state. The fact is mentioned in this place as an answer to questions already brought out in this paper.

<sup>3</sup> The normal non-protein nitrogen of the blood reaches its high level at about 40 mg. per 100 c.c.; 200 mg. per 100 c.c. is an exceptionally high figure with severe nephritis. The difference of 160 mg. per 100 c.c. accounts for 4.8 gms. nitrogen if the blood volume equal 3 liters.

Any further consideration of these facts or endeavors to interpret them would be, with the evidence at hand, idle conjecture.

**CONCLUSIONS.** The retention of nitrogen is one of the common phenomena associated with a large percentage of the cases of nephritis observed in hospitals. Whether this retention characterizes also, in lesser degree and periodically, earlier stages of the disease is not at present clear; but this is generally assumed to be true and is held accountable for some symptoms, whether correctly one may not assert. At those periods of nephritis when patients are forced to seek hospital aid the retention of nitrogen outside of convalescence appears to precede and lead up to either frank uremic manifestations or to the graver complications of renal disease. Furthermore, a careful study of a large number of cases discloses many where the metabolic disturbances seems confined to the protein economy, that is to say, the notable failure in elimination is in respect to nitrogen and this retained nitrogen is found not only in the blood but also in the tissues.

With some of these cases water metabolism is either normal or approximately normal and the total nitrogen elimination then appears to depend directly on the volume of water that passes through the kidneys. This is simply another way of stating an accepted fact: that the diseased kidney can not excrete a concentrated urine, *i. e.*, the power of concentration is impaired. If under these conditions the nitrogen of the diet be reduced to about half the normal and the fluid ingested be increased there results first a sweeping out of retained nitrogen and later normal approximations toward equilibrium. Reduction of nitrogen intake alone does not suffice, nor does the ingestion of large amounts of water if the diet nitrogen be not curtailed.

From a practical point of view this principle would seem to have a therapeutic application, although perhaps of narrow scope.

## **THE DIFFERENTIATION OF NEPHROPATHIES, CARDIOPATHIES, AND ALLIED CONDITIONS.**

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THE diagnosis of renal insufficiency at present rests chiefly on the establishment of a diminished rate of elimination of certain substances normal or foreign to the usual body metabolism. It is

improbable that any single, simple test will ever completely supplant a quantitative study of the water, chloride, and nitrogen balance, especially when this is supplemented by a quantitative test of the rate of elimination under conditions of stress, *e. g.*, 10 grams of sodium chloride, 3 liters of water, or 20 grams of urea added to the diet. To conduct such a metabolism study successfully requires several weeks and necessitates working with a constant or analyzed diet, besides careful separation, collection, preservation, and analysis of the twenty-four-hour urine during the period of study. It imposes, therefore, on the patient, personnel, and analyst conditions which are difficult to realize at present, either in hospital work or in private practice, even in isolated cases, and which are almost excluded as a routine procedure on a large material. It is highly desirable to have some alternative procedure which is more rapid and convenient with as little sacrifice as possible to thoroughness, accuracy, and reliability.

It is well known that the delayed elimination of certain substances in the usual forms of nephritis results eventually in the retention of these substances in the body. At present there is a lack of definite information concerning the quantitative distribution of the retained substances throughout the body fluids and tissues. It is known, however, that an increased concentration of certain substances in the blood serum occurs in many cases of nephritis. Furthermore, the blood serum is the most accessible material to study for evidence of changes in concentration, which would result from retention of sufficient quantities of the substances in question.

Through the work of Widal and his collaborators, of H. Strauss, and of P. v. Monakow, the existence of two definite forms of nephritic retention has been established. In one form water and salt are retained, while in the other there is retention of nitrogenous substances. In some cases both forms of retention occur together. While this information has been derived chiefly from metabolism studies, it would seem logical to suppose that a sufficiently prolonged retention would be followed by characteristic changes in the blood serum. The detection of these changes in the serum would depend largely on a fortunate selection of methods. Chemical methods alone would not always yield the information desired. A determination of the concentration of sodium chloride, for example, would reveal little or nothing if both water and salt were retained in corresponding amounts. Nevertheless, the resulting dilution of the serum with aqueous salt solution could be detected by physical methods. H. Strauss<sup>1</sup> made use of the refractometer for this purpose, and thereby called attention to the hydremic state of the blood serum, as estimated by the low refractive index, in cases of nephritis with edema.

<sup>1</sup> Ztschr. f. klin. Med., 1906, lx, 501.



Other physical methods may be used to detect different changes in nephritic blood serum. The freezing-point, for example, may be taken as a measure of the concentration of relatively simple molecules, irrespective of their chemical nature. Although the freezing-point method has been more or less abandoned of late, previous reliable work has shown that there is an increased depression of the freezing-point of the blood serum in most cases of uremia. Determinations of the specific gravity have also been used to detect changes in the composition of blood serum, and hydremic sera have been recognized previously by this method.

The numerical values of the freezing-point, refractive index, and specific gravity of normal human serum are practically constants. In the pathological sera the freezing-point, refractive index, and specific gravity not only deviate from the normal, but may also vary independently of one another. These independent variations represent changes in the concentration of entirely different groups of substances. Consequently, the systematic use of these methods would seem especially applicable to the problem of nephritic retention, and should yield valuable results in the diagnosis of cardiopathies and nephropathies. This is in fact the case, and it has been possible with these methods to establish characteristic serum pictures for (1) chronic nephritis with edema, (2) chronic nephritis with uremia, and (3) chronic nephritis with both edema and uremia. Furthermore, chronic nephritis with edema may be differentiated from cardiac decompensation with edema by analysis of the serum. Finally, it is possible to recognize a group of cases which cannot be classified either as primary cardiopathy or nephropathy. These cases show persistent hypertension and an extremely concentrated serum.<sup>2</sup> In the absence of more detailed knowledge they may be designated provisionally as cases of primary arteriosclerotic hypertension.

In the present study the determination of the freezing-point, refractive index, and specific gravity have been supplemented by determination of the protein content and dry residue of the serum. While these supplementary determinations do not add materially to the results, they furnish a striking demonstration of the relatively large variations which are possible in the solid constituents of the blood serum in different diseases.

**METHODS.** The *freezing-point* was determined with the Beckmann apparatus. The customary precautions as to supercooling and inoculation were always observed. The determinations were made in duplicate, often in triplicate, and are accurate to 0.002° C. The freezing-point is designated as F. P. The freezing-point of blood serum is always below 0° C., and the numerical values are consequently minus quantities. An increased freezing-point in the text refers to one farther below zero, or with a greater absolute value, than that of normal serum.

<sup>2</sup> W. H. Veil, *Deutsch. Arch. f. klin. Med.*, 1913, cxii, 504; and 1914, cxiii, 226.

The *refractive index* was determined with the Zeiss immersion refractometer. The expression  $\Delta N_d \times 10^3$  represents the difference between the refractive indices of serum and water at the same temperature multiplied by 1000. This makes the numerical results more striking to the eye without affecting their validity in any way.

The *specific gravity* was determined with an Ostwald pycnometer. The figures given are corrected for temperature and buoyancy of air. The specific gravity is designated as sp. gr. in the tables.

Group.	Case.	Freezing-point.	$\Delta N_d \times 10^3$	Specific gravity.	Dry residue.	Protein content.
I. Normals:	1 F	0.55	16.8	1.027	9.5	7.9
	2 B	0.56	17.0	1.026	.....	7.7
	3 R	0.59	17.8	1.026	9.9	8.5
	4 E	0.57	17.9	1.027	.....	.....
	5 F	0.57	18.0	1.027	10.0	8.2
II. Cardiac Decompensation with Edema:	1 H	0.55	19.2	1.030	10.8	9.2
	2 L	0.58	17.3	1.026	9.7	8.0
	3 C	0.56	17.0	1.025	9.5	7.8
	4 H	0.56	16.4	1.024	9.1	7.4
	5 Z	0.53	16.0	1.024	9.1	7.4
	6 H	0.54	16.0	1.024	9.0	7.5
III. Chronic Nephritis with Edema:	1 H	0.59	11.0	1.015	6.3	4.3
	2 H	0.53	11.3	1.016	6.6	5.0
	3 F	0.53	11.5	1.016	6.9	5.1
	4 T	0.55	12.6	1.017	7.1	5.6
	5 K	0.57	12.8	1.020	7.2	6.1
	6 F	0.56	12.8	1.021	.....	5.7
	7 D	0.54	12.9	1.020	7.3	.....
	8 R	0.55	12.9	1.020	7.2	5.6
	9 G	0.56	13.0	1.019	7.6	5.7
	10 V	0.59	13.2	1.017	7.5	.....
	11 P	0.56	13.5	1.019	8.8	5.7
	12 R	0.54	13.5	1.018	7.7	6.0
	13 M	0.55	14.2	1.021	8.0	6.2
	11 R	0.55	14.2	1.022	8.4	6.6
	15 G	0.56	14.3	1.023	8.0	6.3
	16 T	0.55	14.5	1.023	8.1	6.7
	Sept. 28 17 G	0.57	13.1	1.022	7.3	5.8
	Oct. 7 17 G	0.55	14.3	1.022	8.1	6.6
	July 27 18 K	0.55	13.8	1.020	8.1	6.3
	Oct. 7 18 K	0.56	14.8	1.022	.....	6.7
IV. Chronic Nephritis with Uremia:	1 V	0.76	18.9	1.030	10.8	8.3
	2 P	0.68	18.9	1.030	10.7	8.4
	3 C	0.67	18.3	1.027	.....	.....
	11.	0.66	18.2	1.030	11.4	9.0
	5 K	0.62	17.1	1.028	.....	.....
	60 S	0.61	16.5	1.027	11.1	7.8
V. Chronic Nephritis with Edema and Uremia:	1 G	0.61	15.1	1.025	8.5	7.8
	2 P	0.63	11.1	1.022	8.2	5.9
	3 C	0.62	13.3	1.022	7.4	5.3
VI. Arteriosclerosis with Hypertension:	1 G	0.59	20.8	1.033	12.2	9.8
	2 H	0.56	20.7	1.031	11.1	9.4
	3 W	0.56	19.7	1.030	11.6	9.3

The *protein content* was determined gravimetrically after precipitation by alcohol. The *dry residue* was determined in the customary manner. The results of the determinations of the protein content and dry residue are expressed as percentage weight in volume.

Ten to 15 c.c. of serum are sufficient for single determination of the freezing-point, refractive index, specific gravity, protein content, and dry residue.

RESULTS. The results are given in the table on the opposite page. The cases are arranged in groups according to the clinical manifestations. The symptoms and serum pictures of each group will be discussed in detail.

GROUP I. *Normals*. Practising physicians and assistants in the hospital who were in good physical condition served as sources of normal serum.

Serum findings.	Freezing-point.	$\Delta Na \times 10^6$	Specific gravity.	Dry residue.	Protein content.
Average . . . . .	0.57	17.5	1.027	9.8	8.1

The individual variations from the average are very small, less than 4 per cent. in the freezing-point and refractive index, and less than 0.1 per cent. in the specific gravity. The average figures for the normals serve as a basis for comparison with the figures in the pathological groups.

GROUP II. *Cardiac Decompensation with Edema. Clinical Symptoms*. These cases all presented evidence of cardiovalvular disease with decompensation, many with a previous rheumatic history. All had hypertrophied *hearts*, five showing the characteristic enlargement of mitral disease, greatly displaced right heart and conus, and the sixth, mitral and aortic disease and a pericardial effusion which was confirmed by exploration. The *edema* varied from slight puffiness of legs to general edema of the dependent subcutaneous tissues, with fluid in the pleural and peritoneal cavities. The *urine* voided varied in volume from 600 c.c. to 2700 c.c.; average specific gravity, 1.016; all contained albumin in various amounts, and casts were found in 4 cases. The *eye-grounds* were normal in all of them. Five recovered sufficiently to leave the hospital and one died, and the diagnosis of mitral disease was confirmed at autopsy.

Serum findings.	Freezing-point.	$\Delta Na \times 10^6$	Specific gravity.	Dry residue.	Protein content
Average Group II . . . . .	0.55	17.0	1.026	9.5	7.9
Average normal . . . . .	0.57	17.5	1.027	9.8	8.1

The serum is practically normal. The individual variations are somewhat greater than in the normals, and the extremes in this group surpass the extremes in the group of normals. Yet these variations are insignificant. The general average of the group

corresponds closely to the normal average, but is slightly lower throughout.

GROUP III. *Chronic Nephritis with Edema. Clinical Symptoms.* All presented hypertrophy and dilatation of the heart to varying degrees. Systolic murmurs were noted in half the cases. The average blood-pressure was 130, with a maximum of 170 and a minimum of 110. The volume of *urine* varied from 600 c.c. to 3025 c.c.; average specific gravity, 1.019; they all contained albumin and casts; phthalein determinations were made in 4 cases:

1 H	First appearance noted in fifty-two minutes.
5 K	15 per cent. in first hour, 10 per cent. in second hour.
15 G	10 per cent. in first hour, 11 per cent. in second hour.
17 G	58 per cent. in first hour, 15 per cent. in second hour.

*Edema* was present in all cases, varying from pitting of the lower extremities to general subcutaneous edema and fluid in the serous cavities. Five cases showed varying degrees of neuroretinitis. No case presented any mental symptoms.

Serum findings.	Freezing-point.	$\Delta N \times 10^3$	Specific gravity.	Dry residue.	Protein content.
Average group III . . .	0.56	13.2	1.020	7.6	5.9
Average normal . . .	0.57	17.5	1.027	9.8	8.1

The serum in this group presents the characteristic picture of hydremia. With the exception of the freezing-point, all of the figures are much lower than normal. The serum is diluted. The normal values of the freezing-point show that the dilution is not due to water alone and that sufficient salt has also been retained to maintain the normal osmotic pressure.

GROUP IV. *Chronic Nephritis with Uremia. Clinical Symptoms.* The cases all presented very moderate degrees of cardiac hypertrophy. Systolic murmurs were noted in but 2 of the 6 cases. The average blood-pressure was 160, with a maximum of 190 and a minimum of 100. The urinary volume varied from 750 c.c. to 1650 c.c.; average specific gravity, 1.015; albumin was present in large amounts, and many casts were present; phthalein determinations were made in 5 cases:

2 P	Trace at the end of two hours.
3 C	None at the end of two hours.
4 L	None at the end of two hours.
5 K	16 per cent. in first hour, 14 per cent. in second hour.
60'S	16 per cent. in first hour, 3 per cent. in second hour.

Two of the cases presented very slight pitting of the skin over the tibiae, but no fluid was present in the serous cavities. The *eye-grounds* were examined in 5 cases; 3 C and 4 L showed extreme neuroretinitis; in 2 P the retina was obscured by capacity of the

media; in 1 V the left eye was normal and the fundus of the right eye could not be seen; and 60'S was reported normal. Three of the 6 cases had *convulsions*, and all had *mental symptoms*, varying from restlessness and anxiety to active delirium finally resulting in coma and death.

Serum findings.	Freezing-point.	$\Delta N_1 \times 10^3$	Specific gravity.	Dry residue.	Protein content.
Average group IV . . . . .	0.67	18.9	1.029	11.0	8.4
Average normal . . . . .	0.57	17.5	1.027	9.8	8.1

The serum of this group is characterized by a marked increase in the freezing-point and a slight increase in the other figures. This represents a concentrated serum with a relatively large increase in the concentration of the substances which affect the freezing-point.

GROUP V. *Chronic Nephritis with Uremia and Edema. Clinical Symptoms.* This group varies little from the last, except in the presence of edema of the extremities and the serous sacs. There was enlargement of the *heart* in all; dry pericarditis was noted in one of the cases. The average blood-pressure was 170, with a maximum of 200 and a minimum of 115. The urinary volume varies from 600 c.c. to 2200 c.c.; average specific gravity, 1.020; large amounts of albumin and many casts were present; phthalein determinations were made in 2 cases:

1 G	Trace recovered in two hours.
3 C	None recovered in two hours.

The *eye-grounds* in one case showed marked neuroretinitis (old and new); one was normal, and one case was not examined. All presented *mental symptoms* and had *convulsions*. One died, one became improved, and one well enough to discharge from the hospital.

Serum findings.	Freezing-point.	$\Delta N_1 \times 10^3$	Specific gravity.	Dry residue.	Protein content.
Average group V . . . . .	0.62	14.4	1.023	8.0	6.3
Average normal . . . . .	0.57	17.5	1.027	9.8	8.1

The serum of this group presents a combination of the essential features of Groups III and IV. The freezing-point is increased and all other figures are lower than normal. This constitutes the paradox of a dilute serum with an abnormal increase in the concentration of the substances which affect the freezing-point.

The occurrence of this mixed form characterized by the coexistence of hydremia and an increased freezing-point is in thorough accordance with the results of metabolism studies on nephritics with impaired elimination of both salt (and water) and of nitrogen. Occasionally one symptom may dominate the picture to the exclusion of the others. In one of our cases not given in the table the

clinical symptoms and serum findings on admission indicated an advanced chronic nephritis with edema (Group II). As his condition progressed his edema gradually subsided until he became anhydrotic, simultaneous with the development of uremic symptoms which terminated in coma and death. The changes in the clinical symptoms were accompanied by corresponding changes in the serum findings:

	Date.	Freezing-point.	$\Delta N_4 \times 10^3$	Specific gravity.
Flan.	Oct. 6	0.53	14.1	1.024
	Oct. 28	0.61	16.6	1.027
	Nov. 1	0.67	18.4	1.030

GROUP VI. *Arteriosclerosis with Hypertension. Clinical Symptoms.* These cases all presented the same picture of high blood-pressure with cardiac hypertrophy and dilatation, loud aortic second sound, and no murmurs. The palpable vessels were all noted as thickened to varying degrees. The systolic blood-pressures were 190, 220, and 215. The volume of *urine* was good in all cases; average specific gravity, 1.020; small amounts of albumin were present, but no casts were noted; phthalein determinations were made on all:

1 G	27 per cent. in first hour, 24 per cent. in second hour.
2 H	30 per cent. in first hour, 21 per cent. in second hour.
3 W	60 per cent. in first hour, 19 per cent. in second hour.

In all cases large, tender livers were noted. There was slight edema over tibiae in two cases, none in the third, and the serous cavities were free of fluid. The eye-grounds of two cases were examined; one was normal and the other showed moderate neuritis with tortuous vessels.

Serum findings.	Freezing-point.	$\Delta N_4 \times 10^3$	Specific gravity.	Dry residue.	Protein content.
Average group VI	0.57	20.1	1.031	11.7	9.5
Average normal	0.57	17.5	1.027	9.8	8.1

This group is characterized by a marked increase in the concentration of protein in the serum. The freezing-point is normal, but all other figures are extremely high, chiefly on account of the increased concentration of serum protein.

CONCLUSIONS. The foregoing results demonstrate the practical value of this system of analysis in differentiating the cardiopathies from the nephropathies and in classifying the nephropathies. The diagnostic results thus obtained should correspond closely to the results obtained by a study of the metabolism balance. Determination of the freezing-point, refractive index, and specific gravity of blood serum is a simple procedure and requires at most two hours, while a study of the metabolism balance covering the same

ground would take at least a week. Analysis of serum by these methods possesses other advantages over the metabolism method. Retention of nitrogen or of water and salt is common to a variety of conditions, and is not necessarily indicative of nephritis. Serum analysis enables one to differentiate the cases in which retention is the result of defective renal elimination from those in which retention is due to other causes.

On the other hand there are limitations to the serum work. It is obvious that the retention of any substance must attain a certain threshold figure with respect to time and quantity before any changes could be detected in the serum by these methods. It is conceivable that a slight retention could be detected by the metabolism method before definite changes occurred in the serum. The metabolism method and serum analysis should be used to supplement each other until sufficient comparative data have been obtained.

It should also be borne in mind that the serum findings merely give a picture of the state of the serum at the time of examination. In pathological cases this picture may change from time to time with the progression or regression of the correlated symptoms. A uremic attack may clear up after several weeks either spontaneously or as a result of bleeding and restriction of protein in the diet, and the freezing-point may then return to normal. Similarly an hydremic serum may gradually change to normal during the disappearance of nephritic edema.

Serum analysis as well as the metabolism method also furnishes valuable indications as to the course of dietetic *therapy* to be followed in the different forms of nephropathies. In the uremic type a restriction of protein to the minimum necessary for maintenance is clearly indicated; at the same time the general nutrition should be kept up by increasing the fat and carbohydrate in the diet. In the hydropic form of nephropathy restriction of salt is indicated. Bleeding is beneficial in either uremic or hydropic cases. The restriction of salt or protein in the diet relieves the kidney of unnecessary work and rests the damaged function. No one would expect such treatment to remove scar tissue from the kidney or restore destroyed structures. It may be possible, however, to prevent a progression of the destruction of renal substance and to restore the function of partially damaged structures. At present it is impossible to foresee the beneficial results which may be derived from the dietetic treatment of early cases of chronic nephritis. It is not unreasonable to suppose that similar results would be obtained as in the rational dietetic treatment of diabetes.

## THE RELATION BETWEEN FUNCTIONAL TESTS AND THE PATHOLOGICAL ANATOMY OF THE KIDNEY IN CHRONIC NEPHRITIS.

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Is it possible to tell during life what type of chronic nephritis from the pathologists' view-point is present in the individual case?

Before taking up that question it is important to define what is meant by chronic nephritis and what classification from the pathologists' view-point is the most satisfactory.

It seems most reasonable to consider as chronic nephritis any progressive destruction of the kidney parenchyma resulting from either some infectious agent or some bacterial, metabolic, or chemical poison. The process may start insidiously or follow some outspoken acute disturbance in the kidney. In some cases more than one cause may be present. In other cases a primary injury to the kidney by bacteria or other toxins may upon healing leave too little kidney substance to carry on renal function, so that gradually the remaining kidney tissue goes to pieces under the strain of its routine work. It must also be remembered that acute injury to the renal parenchyma may heal with scar formation and still have the remaining portions of the kidney function normally without any progressive degenerative changes starting in the kidney. Examples of such a condition vary from the isolated sclerosed glomeruli occasionally observed in children's kidneys up to the extensive scarring seen following acute bacterial infections which have healed. Such cases should be looked upon by both pathologist and clinician as healed nephritis and not chronic nephritis.

Although it is evident from the above that chronic nephritis covers a large field of renal conditions, this study will be simplified by leaving out of consideration those cases of chronic nephritis due to the presence of infective agents in the kidney. Certain of the cases reported may have been examples of a chronic nephritis starting upon the scarred kidney resulting from the healing of such an infection.

This work, therefore, narrows itself down to a consideration of those types of chronic nephritis which are usually met with in the medical wards of a hospital that come to a fatal termination. It must be remembered that the amount of kidney destruction in chronic nephritis varies considerably with the duration of the process, and that we rarely have a chance to study at autopsy the cases in the early stages of the progressive kidney disease.



In turning to a pathological classification for chronic nephritis one naturally meets most frequently the old terms chronic parenchymatous nephritis and chronic interstitial nephritis. The application of these terms to clinical conditions and in pathological studies has been rather loose. Furthermore, they do not suggest in the name what is the fundamental lesion in the kidney.

In Mallory's<sup>1</sup> recent book, the classification of nephritis for this group of cases is taken up from the view-point of what part of the kidney tissue is primarily involved. From the name, therefore, one may learn the original focus of the renal involvement, and from that realize just what has been going on in the kidney from the time of the original injury down to the end result.

Mallory, in this classification, speaks of tubular nephritis, capsular-glomerulonephritis, intracapillary-glomerulonephritis, and vascular nephritis. The lesions in any kidney may be of one type or a combination of several types. He mentions a variety of acute lesions which may occur in the first three of these types in that part of the kidney specified in the name. Some of these acute lesions heal without producing a permanent injury in the kidney. Many of them, however, on healing produce a permanent scar in the kidney with subsequent progressive degeneration of the renal parenchyma.

The types of acute nephritis which on healing are apt to turn into a chronic progressive nephritis are certain forms of the acute capsular-glomerulo and the acute intracapillary-glomerulo. It is the early stages of these types of progressive kidney destruction which are commonly considered clinically as chronic parenchymatous nephritis.

The chronic vascular nephritis usually results from simple arteriosclerosis of the smaller renal arteries, but may follow some acute lesion of the smaller renal vessels which upon healing causes impaired circulation with resulting progressive lesions in the vessels and renal parenchyma.

In the chronic vascular type secondary changes take place in the glomeruli supplied by the involved vessels, with eventual sclerosis of all or a part of the tuft. In the two glomerulo types usually the greater number of the glomeruli are involved, with eventual sclerosis of part or all of the capsules or tufts of both. In all three of the types following the injury to the glomeruli, secondary degenerative changes occur in the tubules. These may consist of atrophy and disappearance of the tubules or dilatation with atrophy of the lining epithelium.

Mallory is uncertain whether any actual proliferation takes place in the connective tissue of the kidney, but feels there is certainly a relative increase as the parenchyma disappears. The connective tissue is frequently invaded with cells of the lymphocytic series.

<sup>1</sup> Principles of Pathological Histology, 1914.

In this study the classification of nephritis suggested by Mallory has been followed, as it seems to be much more comprehensive than the older classifications. It was surprising how readily one could put the kidney into the proper group from examination of a single section under the microscope. Dr. Mallory has been kind enough to go over the slides and confirm the group into which each kidney belongs.

Up to the present time eighteen cases of chronic nephritis have come to autopsy at the Peter Bent Brigham Hospital, upon which enough clinical work has been done to make them of interest for comparison between the clinical and anatomical findings.

Unfortunately, as most of the cases were naturally seriously ill, it was not possible to put them on standard diets and learn their ability to put out added salt and urea which have been found at this hospital<sup>2</sup> to be of value in diagnosis and prognosis respectively of chronic nephritis. In most of the cases, however, the following four tests for diagnosis and prognosis of chronic nephritis were carried out: Examination of urine for albumin or casts, blood-pressure determinations, phenolsulphonaphthalein excretion test, and estimation of non-protein nitrogen in the blood. In addition to reporting the results of these tests, record has been made of the age of the patient, the presence or absence of edema at the time of entrance, the examination of the eye-grounds, the previous acute infections, the result of the Wassermann serum reaction, and any complicating conditions at the time of death. This data was obtained from the medical records of the hospital.

It also seemed of interest to note the gross pathological findings at autopsy in order to see if it were possible to place these cases in their proper groups without the aid of the microscope. For this purpose the weight of the two kidneys, the width of the cortex, the adherence of the capsule, and the appearance of the surface of the kidney under the capsule were noted. This data was obtained from the pathological records of the hospital.

All this data is presented in the form of two tables, one containing the cases of chronic vascular nephritis, the other the cases of chronic glomerulonephritis. Most of the glomerulo cases were a combination of capsular-glomerulo and intracapillary-glomerulo. It is evident the majority of the cases are of the chronic vascular type.

Of the 14 cases considered as chronic vascular nephritis 1 was possibly a congenital malformation of the kidney and 2 were possibly healed acute infections which had involved other parts of the kidney besides the vessels and in which progressive renal destruction was going on. The weight of the kidneys varied from 360 grams to 42 grams. The capsule was adherent in 6 and stripped

<sup>2</sup> Frothingham, The Value of Certain Tests for Diagnosis and Prognosis in Chronic Nephritis, *AMER. JOUR. MED. SCI.*, June, 1915.

easily in 8. The surface of the kidney was granular or rough in 12 and smooth in 2. The cortex varied from 8 mm. to 1 mm. In the 4 cases of chronic glomerulonephritis one showed the process in its early stages probably not more than a few weeks or months. The weights varied from 435 grams to 155 grams. In 3 the capsule stripped easily, in 1 there was a slight resistance. The cortex varied from 11 mm. to 4 mm. The surface was smooth in 3 and granular in 1. It is thus evident that the kidneys can not be put with certainty into the proper group from the gross appearance alone. However, in the glomerulo type the capsule usually strips readily, leaving a smooth surface, while in the vascular type the surface is usually granular and the capsule more apt to be adherent.

All but 2 of the cases of chronic vascular nephritis showed albumin on the first or second examination of the urine, and these 2 occasionally did; 3 showed no casts on repeated examinations; 3 showed them only rarely, and the others showed casts pretty constantly. The blood-pressure on entrance in all cases but two was above 150 mm. of mercury. The pulse pressures varied from 100 to 40 mm.

In none of the 13 cases in which the 'phtalein test was done was the elimination for two hours above 40, and several showed no excretion in that time. The non-protein nitrogen of the blood was estimated in 11 of the cases, and in all but one was elevated above 30 mgm. per 100 c.c., which is considered normal when estimated by the Folin and Denis method. In some cases it went as high as 250+ mgm. per 100 c.c. of blood. These very high estimations were found in the blood usually just a short time before death, and probably represent a sudden terminal rise in non-protein nitrogen, which has frequently been noted in the last days of life in cases which have shown pronounced uremic symptoms for some time. Edema was present in 8 cases and absent in 6. In 6 of the 8 cases with edema, myocarditis was recorded as a complicating factor. In 5 of the 11 cases of chronic vascular nephritis in which eye-grounds were examined, no lesions were noted. In the other 6 there was edema, hemorrhages, or exudate, and in some all three. In 2 cases the Wassermann serum reaction was positive. In this group the ages varied from twenty-four to seventy-one years.

In the group of chronic glomerulonephritis albumin and casts were present in all cases. The blood-pressure was elevated above 150 mm. of mercury in 2 and not in the others. The pulse pressure varied from 80 to 45 mm. The phenolsulphonephthalein output was diminished in all 4 cases ranging from 22 in one and a half hours to 0 in two hours. In only 2 cases was the non-protein nitrogen of the blood estimated, and in those 2 it was above 100 mgm. per 100 c.c. Edema was present in 2 cases and absent in 2. In the 2 cases with edema there was no evidence of chronic cardiac

## CHRONIC VASCULAR NEPHRITIS.

Hos- pital No.	Kidney.	Age	Urine.		Blood- pressure.	Pulse	Per cent. phtha- lein in 2 hrs.	Mgms. nitrogen per 100 c.c.	Edema.	Eye grounds.	Wasser- mann re- action.	Past acute infections.	Complications.
			Albu- min.	Cast- s.									
	Wht. of loft												
	Gm. mm.												
328	Very rough	61	+	+	170 110	60	31.0	-	+	No edema. No Not done. Measles, pertussis, Myocarditis. smallpox and acute rheumatism			
673	Rough	32	+	Rare	180 125	55	0	200	0	Not done	++	Measles, osteomyelitis with 7 operations	Fibrous pericarditis.
655	Rough	30	+	+	230 140	90	28.0	90	0	Hemorrhages; ex- Negative udate; no edema		Dobie itch, dysentery, frequent tonsillitis.	None.
805	Granular	50	Rare	0	205 130	75	0	100	+	No edema; no Negative hemorrhage; no exudate		Measles, chicken-pox. None. pertussis, bilious at- tacks	
1124	Finely granular	63	+	+	130 80	50	34.0	62	+	No edema; no Negative hemorrhage; no exudate		Measles, mumps, per- tussis, scarlet fever, acute rheumatism	Myocarditis; aortic insufficiency.
4	Rough	63	+	+	240 140	100	12.0	-	0	Exudate; no hem- Negative orrhage; no edema		None recorded	None.
1640	Granular	24	+	0	120 68	52	0	204	0	No exudate; no Negative hemorrhage; no edema		Measles, pertussis, chicken-pox, scarlet malformation of fever, sore throats kidney.	
1593	Rough	31	+	+	238 138	100	3.0	56 to 138	0	Edema; exudate; Negative hemorrhage		Measles, pertussis, chicken-pox, scarlet fever, typhoid. Con- vulsions at age (8-10) Measles, erysipelas, ty- phoid	None.
1975	Smooth	39	+	+	208 152	56	-	257.7	+	Edema; exudate; Negative hemorrhage		Measles, malaria	Myocarditis, auricu- lar fibrillation, hem- iplegia.
1844	Rough	71	Rare	Rare	155 95	60	17.0	25	+	Not done		Measles, acute rheu- matism, gonorrhea, arter- iosclerosis.	
1405	Granular	59	+	Rare	175 130	45	40.5	-	+	Not done		Measles, acute rheu- matism, gonorrhea, arter- iosclerosis.	

2006 Smooth 330 1.5 Strips easily 45 + + 190 95 92 0 80 0 No edema; no exudate; no hemorrhages + Marked anyloid in scarlet fever, measles, whooping cough, mumps, typhoid regurgitation

2111 Granular 220 2.5 Strips easily 52 + 0 180 120 60 10.0 Urea 55.5 + Slight edema; no hemorrhages; no exudate Negative

2108 Granular 284 Markings vague 28 + + 190 130 40 22.0 47.5 + Edema; exudate; slight hemorrhage Negative

Croup as a baby, moderately old, healed in years ago. Dull red tracillary glomerular lesion.

## CHRONIC GLOMERULONEPHRITIS.

81	Smooth	435	11.0	Strips easily	26	+	+	140	85	55	22 in. 1 1/3 hrs.	-	+	Not done	Chorea, some septic or tubercular chest condition, grippé	Sub-acute nephritis of the intracapillary type.
251	Smooth	314	8.0	Strips easily	38	+	+	160	115	45	4.0	-	+	Slight edema; no hemorrhage; exudate	Scarlet fever, typhus, rheumatic fever, ovary operation	Pneumonia. Pericarditis, pleurisy, cystitis. Both intracapillary and capsular types.
1283	Granular	155	4.0	Slightly adherent	16	+	+	140	85	55	0	117	0	No exudate; no hemorrhage; edema.	Measles, mumps, diphtheria, scarlet fever, chicken-pox, sore throats, pertussis	None. Both intracapillary and capsular types.
1800	Smooth	340	9.0	Strips easily	19	+	+	195	115	80	Trace	112	0	No edema; no hemorrhage; exudate	Scarlet fever, measles, scarlet media, frequent sore throats	None. Intracapillary type.

disease. In 3 of the cases of chronic glomerulonephritis the eye-grounds were studied, and except for slight edema in one no abnormal findings were noted. The Wassermann serum reaction was negative in the 3 cases in which it was done. The ages of these 4 cases ranged from thirty-eight to sixteen years, which is lower than those of the other group. There were, however, many cases of the vascular type within these age limits.

From a study of this small group of cases of chronic glomerulonephritis it is evident that it will not be possible by means of the four tests for renal disease mentioned above to tell definitely into which group a given case of nephritis belongs. The age of the patient, the presence or absence of edema or pulse pressure also does not give any assistance in this direction. Changes in the eye-grounds were not constant enough in either group to aid in classifying the cases. The previous history is not of assistance, for although most of the cases of glomerulonephritis had scarlet fever, still many of the cases of chronic vascular nephritis that died young also had had scarlet fever. It must be remembered that these cases are all ones of pronounced nephritis in the end stages. It is possible that by the more complicated dietary tests for renal function which may be carried out on the patients not so ill a grouping of the cases according to the pathological lesions may be accomplished. Possibly, therefore, at some future date enough of the chronic nephritis cases that have been studied in this hospital by these more elaborate methods will come to autopsy here to settle this question.

Grouping all these cases for clinical purposes simply as chronic nephritis of a severe grade, it is interesting to note that the non-protein nitrogen of the blood was elevated in all cases but one in which it was examined, and that one may well have died of cardiac and cerebral complications. The ability of the kidney to excrete phenolsulphonephthalein was diminished in all the cases in which it was done. Albumin was present in the first or second urine examinations in all cases but 2. Casts were not found in 3 cases and only rarely in 3 more. The blood-pressure was above 150 in all but 4 of the cases; 7 of the 14 cases in which the fundi were examined showed lesions in the eye-grounds.

# THE RELATIONSHIP OF THE PATHOLOGICAL HISTOLOGY AND THE IODIN COMPOUNDS OF THE HUMAN THYROID.\*

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THE present study presents some new evidence in the solution of the problems of the relationships between the clinical, pathological, and chemical findings in cases of human goitre. The scope of the study is limited to 566 cases, from which specimens have been analyzed chemically in the course of a general investigation of the iodine compounds of the thyroid. The cases were not selected, but were taken at random in the order as operated on from the patients under treatment in the Mayo Clinic during 1914.

**CLINICAL CLASSIFICATION.** The clinical classification of the cases into (1) hyperplastic toxic ("exophthalmic" goitre); (2) non-hyperplastic toxic with high blood-pressure; (3) non-hyperplastic toxic with low blood-pressure; (4) non-hyperplastic questionably toxic with low blood-pressure, and (5) non-hyperplastic atoxic with low blood-pressure has been made by Plummer,<sup>1 2</sup> and follows his previous grouping. Though the terms "hyperplastic" and "non-hyperplastic" refer to the morphology of the gland, which cannot be shown until its removal, yet they have been used in making the clinical diagnoses by Plummer and his associates with but a negligible margin of error, as shown by the subsequent pathological examination.

**PATHOLOGICAL CLASSIFICATION.** The pathological classification is, with slight modification, that previously published by Wilson.<sup>3-10</sup> The main divisions, (1) primary hypertrophy and hyperplasia of epithelium; (2) primary retention of colloid with atrophy of epithelium; (3) encapsulated adenomas, and (4) carcinomas, with their several subdivisions, are self-explanatory. As our study of the morphology of the thyroid in goitre has progressed, it has been found desirable to subdivide the group of regressing hyperplasias into subgroups, early, advanced, and very advanced regression. Also the undegenerated encapsulated adenomas, with colloid-filled acini, Group G, are so few in proportion to the degenerated adenomas, Group F, that in the present study the three subgroups have not been separated. The encapsulated adenomas have been separated from adenomatoses, and the latter

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included in the group described as primary retention of colloid with atrophy of epithelium.

**CHEMICAL INVESTIGATION.** The methods employed in the determination of iodine and the dry weight of thyroid substance removed at operation were as follows:

The fresh gland was placed in a crystallizing dish, covered with a glass plate, and heated three or four hours in an oven at 100° C. This preliminary treatment removed a large portion of the water and made the gland cut more easily into smaller pieces. After the gland was cut into small pieces it was completely dried in a vacuum desiccator, and then ground to a fine powder in a coffee mill, thoroughly mixed, and the iodine content determined<sup>11</sup> in a one-half gram portion. Two modifications of this procedure were employed for some of the glands. Instead of taking the entire fresh gland for purposes of desiccation, a known portion of the total was taken, and from the dried weight of this portion the dried weight of the total gland and the amount of iodine were calculated. The other modification consisted in taking a portion of the gland after it had been fixed in 4 per cent. formaldehyde. From this known portion the dried weight of the total gland was determined, and the total iodine based on this weight. Analysis of the formaldehyde solution showed that in every case an appreciable amount of iodine from the gland had passed into the formaldehyde solution. It was therefore necessary to determine the amount of iodine in this solution to obtain the total iodine originally present in the portion of the gland removed at operation. The results obtained by these procedures were kept separate until after they were compared with the pathological grouping. This comparison showed no appreciable differences between the three methods, so that in the final tabulation of results there was no discrimination made as to which method was employed for determining the total dried weight and the total iodine.

In addition to the determination of the total iodine, the dried thyroid substance of fifty-eight thyroids was hydrolized by a method already published.<sup>13</sup> This hydrolysis splits the proteins into simpler products and divides the total iodine into two chemically different groups. The  $\alpha$ -iodine compound is insoluble in acids. The  $\beta$ -iodine compound is soluble. Both  $\alpha$ - and  $\beta$ -iodine are in organic combinations, and there is evidence that  $\beta$ -iodine is not a decomposition product of the  $\alpha$ -iodine compound, but that the two forms exist independently in the gland. Physiological tests<sup>14</sup> have shown that the  $\alpha$ -iodine compound produces the typical effects of desiccated thyroid, but that the  $\beta$ -iodine compound has no toxic action. It therefore seemed desirable to determine the amount of  $\alpha$ -, or toxic, iodine compound in some of the glands removed. For the determination of the amount of  $\alpha$ -iodine in a given gland, the dry



powdered gland was boiled in 90 per cent. alcohol in the presence of 1 per cent. sodium hydroxide for forty-eight hours, 2.5 grams of the dried thyroid per 100 c.c. of alcohol. At the end of the boiling, carbon dioxide was passed through the solution and the alcohol evaporated. The solution was then acidified with 20 per cent. sulphuric acid. The precipitate ( $\alpha$ -constituents) was filtered and washed with a small amount of water. This precipitate was dissolved in sodium hydroxide. The amounts of iodine in the filtrate ( $\beta$ -constituents) and in the solution of the  $\alpha$ -constituents were determined. This gave the amounts of  $\alpha$ - and  $\beta$ -iodine, and the sum of these two the total iodine in the gland.

In connection with the determination of iodine, it may be said that the results obtained during the course of this investigation approximate 4000 determinations of iodine. From a comparison of duplicates and an inspection of the accuracy of the total series, it would appear that for this work the method used is entirely adequate. The great advantage of obtaining a perfect "blank" where no iodine exists, of having no blue color flashed back from the starch iodine reaction after titration is finished, and the wide range in the amounts of iodine which come within the method, together with the shortness of time and inexpensive chemicals, have made this method the one of choice in our laboratory.

PROTOCOLS. The bulk of the material makes publication of protocols obviously cumbersome. However, the protocols of the chemical analyses and pathological examinations, with the microscopic sections, gross specimens and the clinical histories are on file in the Mayo Clinic, and are open to study to anyone interested. The results have been accurately compiled and condensed into a series of tables herewith presented.

DISCUSSION OF TABLES. *Table I.* The distribution of the cases into the several clinical and pathological groups is given in totals, rather than in averages, that the numbers may serve as a basis for determining the percentage values in subsequent comparisons. It will be observed that the number of cases in certain groups (*A*, hyperplastic toxic; *D*, non-hyperplastic toxic and non-hyperplastic questionably toxic; *II+F*, non-hyperplastic toxic and non-hyperplastic questionably toxic; *F*, questionably toxic; and the carcinomas) are so small as to make the averages of relatively little value. However, it would have been more inaccurate to omit these cases entirely, and attention will be called to the insufficient evidence presented in these groups as the several comparative tables are discussed later. It should be noted that of the 425 cases of non-hyperplastic goitre, 197 presented symptoms which might have caused many of them to be diagnosed as "exophthalmic goitres" by clinicians elsewhere. Without analyzing in detail the distribution of these cases, it may be pointed out that the general distribution

## GOTTES, CORRELATION OF PATHOLOGICAL, CLINICAL AND CHEMICAL DATA

TABLE I.—NUMBER OF CASES.

TABLE II.—AVERAGE AGES (IN YEARS).

## CLINICAL CLASSIFICATION.

1. Hyperplastic toxic ("exophthalmic" goitre).

2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).

3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

4. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).

Totals (averages).

1. Hyperplastic toxic ("exophthalmic" goitre).

2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).

3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

4. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).

Totals (averages).

## 1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:

- A. Early hypertrophy and hyperplasia . . . . .  
 B. Advanced hyperplasia . . . . .  
 C 1. Early regression of hyperplasia . . . . .  
 C 2. Advanced regression of hyperplasia . . . . .  
 C 3. Very advanced regression of hyperplasia . . . . .

## 2. PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:

- D. Secondary regeneration of epithelium . . . . .  
 H. Diffuse atrophy of epithelium . . . . .  
 H + F. Diffuse atrophy of epithelium with included adenomas . . . . .

## 3. ENCAPSULATED ADENOMAS:

- E, F, G . . . . .

## 4. CARCINOMAS . . . . .

Totals (average) . . . . .

Totals (averages).

1. Hyperplastic toxic ("exophthalmic" goitre).

2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).

3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

4. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).

Totals (averages).

closely approximates that shown in a similar group of patients operated on in 1911 and 1912.<sup>9</sup>

*Table II.* Table II shows the average age of the patients at the time their thyroids were removed. While the average ages of the patients with hyperplastic toxic goitre is thirty-five years, it will be noted that the average age of those with early hypertrophy is only nineteen years, of those with advanced hyperplasia thirty-four years, and of those whose thyroids showed regression in the hyperplastic process it is thirty-eight, thirty-five and thirty-four years respectively, in inverse order to the amount of regression. At first thought, it would appear that this inversion of the average ages in relation to the amount of regression of hyperplasia is contradictory, but when the average ages are examined in the light of Table III, in which is shown the average duration of goitre in months, it will be seen that while the younger patients showed the greatest amount of epithelial regression the duration of the goitre as well as the duration of symptoms were both also inversely as to age and directly as to the amount of regression. The same holds good in the four cases of clinically hyperplastic toxic goitre with secondary regeneration of the thyroid epithelium. Here the average age was twenty-nine years, and though the average duration of goitre was one hundred and thirty-two months, the average duration of symptoms was only eleven months. In this pathological group (epithelial regenerations) the age-distribution of the patients in the various clinical classes is interesting, being twenty-nine years in the hyperplastic toxic, forty-five years in the non-hyperplastic toxic with high blood-pressure, fifty years in the non-hyperplastic toxics with low blood-pressure, thirty-three years in the non-hyperplastic questionably toxic, and thirty-two years in the non-hyperplastic atoxic cases.

The somewhat erratic age distribution of the cases in which the glands showed encapsulated adenomas, either alone (*E, F, G*) or included in diffuse colloid goitres (*H+F*), may not be wholly accidental, but may be due to the influence of the neoplasms. This point, however, is still under investigation in a larger series of cases.

*Table III.* The average duration of goitres in months for the entire series and the duration of hyperthyroidism in months for the hyperplastic series is shown in Table III. The duration of the symptoms in the toxic non-hyperplastic cases is so difficult to determine with any degree of accuracy from the patient's description that no attempt has been made to state it in months. The difference between the period of duration of goitre in hyperplastic toxics, averaging forty-one months, and the period of duration of goitre in the non-hyperplastic groups (the lowest of which is 156 months, and the highest 276 months, with an average of 192 months) is very marked, and constitutes a point in clinical diagnosis.

## GOITRES, CORRELATION OF PATHOLOGICAL, CLINICAL AND CHEMICAL DATA

TABLE III.—AVERAGE DURATION OF GOITRES AND AVERAGE DURATION OF TONIC SYMPTOMS (IN MONTHS).

TABLE III.—AVERAGE DURATION OF GOITRES AND AVERAGE DURATION OF TOXIC SYMPTOMS (IN MONTHS).									
PATHOLOGICAL CLASSIFICATION.		CLINICAL CLASSIFICATION.					Totals (averages).		
		1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic (?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).			
PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:		9 (9)					9 (9)		
A. Early hypertrophy and hyperplasia		17 (10)					17 (10)		
B. Advanced hyperplasia		32 (18)					32 (18)		
C 1. Early regression of hyperplasia		53 (35)					53 (35)		
C 2. Advanced regression of hyperplasia									
C 3. Very advanced regression of hyperplasia		68 (47)					68 (47)		
PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:		132 (11)	216	276	204	156	209	148	
D. Secondary regeneration of epithelium		..	240	180	240	168	204	..	
H. Diffuse atrophy of epithelium		..	216	156	240	168	180	..	
H + F. Diffuse atrophy of epithelium with included adenomas		..							
3. ENCAPSULATED ADENOMAS:		..	180	180	192	156	168	..	
E, F, G		..	192	—	—	300	252	..	
4. CARCINOMAS <td>..</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>		..							
Totals (averages)		41	228	180	216	168		143	

TABLE IV.—AVERAGE SYSTOLIC BLOOD-PRESSURE.									
PATHOLOGICAL CLASSIFICATION.		CLINICAL CLASSIFICATION.					Totals (averages).		
		1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic (?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).			
PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:		140					140		
A. Early hypertrophy and hyperplasia		138					138		
B. Advanced hyperplasia		147					147		
C 1. Early regression of hyperplasia		132					132		
C 2. Advanced regression of hyperplasia									
C 3. Very advanced regression of hyperplasia		144					144		
PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:		120	164	129	120	125	120	125	140
D. Secondary regeneration of epithelium		128	171	130	128	120	128	120	141
H. Diffuse atrophy of epithelium		132	176	121	132	124	132	124	143
3. ENCAPSULATED ADENOMAS:		126	171	129	126	128	126	128	144
E, F, G		—	157	—	—	120	—	120	142
4. CARCINOMAS		127	171	128	127	123	127	123	
Totals (averages)		127	171	128	127	123	127	123	

The maximum severity of symptoms, and the severity at the time of examinations in the several groups of hyperplastic toxic cases, indicated on a scale of 1, 2, 3, 4, and 5, averaged as follows:

	Maximum severity.	At time of examination.
A Early hypertrophy . . . . .	1.0	1.0
B. Advanced hyperplasia . . . . .	2.6	2.5
C 1. Early regression . . . . .	3.2	2.4
C 2. Advanced regression . . . . .	3.6	2.5
C 3. Very advanced regression . . . . .	3.4	2.0

*Table IV.* The discussion of the systolic blood-pressure as presented in Table IV will be covered *in extenso* by Plummer.<sup>16</sup> It is included in the present paper only for reference in relation to the percentage of iodine and total amount of iodine in the portion of removed gland. (See Tables VI and VII.)

*Table V.* The average weight of the portion of the gland removed at operation in the hyperplastic toxic group was 57 grams, as compared with 55 grams, the average weight of the removed portion in the 1911 and 1912 cases.<sup>9</sup> The average weight of the removed portion of the 425 cases of non-hyperplastic thyroids was 168 grams, as compared with 171 grams, the average weight of the non-hyperplastics in the 1911 and 1912 series.<sup>9</sup> This is of significance in showing the great disparity in size between the thyroids from hyperplastic toxic and those from non-hyperplastic toxic cases as previously noted.<sup>3,9</sup> In the individual groups the removed portion of gland is larger in the cases of high blood-pressure than in the several pathological groups with low blood-pressure.

*Table VI.* The variation in the percentage of iodine in the dried gland in the several histological types of thyroids from hyperplastic toxic cases is most marked. Starting in with the cases of early hypertrophy, the percentage is 0.11. It drops thence to 0.03 in the advanced hyperplasias, rises to 0.07 in the early regressions, to 0.16 in the advanced regressions, and to 0.19 in the very advanced regressions. A comparison of these percentages with those showing percentages of iodine in the various non-hyperplastic thyroids shows that in no subgroup of the latter division does the percentage of iodine rise as high as that in the thyroids from cases with advanced regression in hyperplastic glands.

In the pathological groups of the non-hyperplastic series the secondary regenerations (type D) present both the highest and the lowest percentages aside from certain low averages in the encapsulated adenomas and the carcinomas. The diffuse epithelial atrophies (type H) vary the least. The encapsulated adenomas which generally low vary from 0.02 to 0.07.

In the individual clinical groups, it is interesting to note that in all, except the adenomas, the percentage of iodine is highest (av. 0.1 per cent.) in the non-hyperplastic toxic cases with low blood-pressure. The next in amount are the cases of non-hyperplastic toxic with high blood-pressure (av. 0.08 per cent.). In general,

## GOTTERS, CORRELATION OF PATHOLOGICAL, CLINICAL AND CHEMICAL DATA

TABLE V.—AVERAGE WEIGHT OF REMOVED GLAND (FRESH) IN GRAMS.

TABLE VI.—AVERAGE PER CENT. OF IODIN IN DRIED THYROID.

## PATHOLOGICAL CLASSIFICATION.

1. Hyperplastic toxic ("exophthalmic" goitre).

2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).

3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

4. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).

5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).

Totals (averages).

## 1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:

- A. Early hypertrophy and hyperplasia . . . . . 46  
 B. Advanced hyperplasia . . . . . 50  
 C 1. Early regression of hyperplasia . . . . . 56  
 C 2. Advanced regression of hyperplasia . . . . . 53  
 C 3. Very advanced regression of hyperplasia . . . . . 70

## 2. PRIMARY RETENTION OF COLLOID ATROPHY OF EPITHELIUM:

- D. Secondary regeneration of epithelium . . . . . 175  
 H. Diffuse atrophy of epithelium . . . . . 223  
 H + E. Diffuse atrophy of epithelium with included adenomas . . . . . 189

## 3. ENCAPSULATED ADENOMAS:

- E, F, G . . . . . 109  
 . . . . . 730

## 4. CARCINOMAS

Totals (averages)

46

59

56

53

70

159

181

179

114

583

137

175

223

189

109

730

190

150

167

157

114

140

583

137

171

158

183

108

140

157

171

158

183

108

140

157

114

140

583

137

0.11

0.03

0.07

0.16

0.19

0.07

0.08

0.09

0.07

0.005

0.10

0.08

0.06

0.06

0.06

0.085

0.11

0.03

0.07

0.16

0.19

0.07

0.08

0.09

0.07

0.005

0.10

0.08

0.06

0.06

0.06

0.085

0.11

0.03

0.07

0.16

0.19

0.07

0.08

0.09

0.07

0.005

0.10

0.08

0.06

0.06

0.06

0.085

0.11

0.03

0.07

0.16

0.19

0.07

0.08

0.09

0.07

0.005

0.10

0.08

0.06

0.06

0.06

0.085

the percentage is lowest in the non-hyperplastic atoxic (av. 0.06 per cent.). Attention is called to this inversion of the order of the percentage amounts in relation to clinical symptoms over those observed in the cases of hyperplastic goitre.

A tabulation of both groups of non-hyperplastic toxic cases in comparison with the non-hyperplastic atoxic cases shows that in 84 per cent. of the atoxic the percentage of iodine was under 0.1, while but 68 per cent. of the toxic cases were under 0.1.

*Table VII.* In the hyperplastic toxic cases, the total amount of iodine in the portion of the gland removed follows the percentage of iodine since the portion of gland removed in these cases is fairly equal in the several groups. The amount averages 9.2 mg. in early hypertrophy, drops to 3.4 mgs. in the advanced hyperplasias, rises to 8 mgs. in the early regressions, to 14.2 mgs. in the advanced regressions, and to 21.9 mgs. in the very advanced regressions. The total amount in the cases with secondary regeneration of epithelium, which showed symptoms placing them in the hyperplastic toxic clinical group, is the smallest of any of the groups except the advanced hyperplastic toxics and carcinomas.

In the non-hyperplastics, the largest amount is in the toxics with low blood-pressure (23.8 mgs.), while in the atoxics the amount averages 15 mgs. It should be noted that though the amount of iodine in the portions of glands removed in the non-hyperplastic cases is greater than the amount removed in the hyperplastic cases, the comparison of the relative amounts in the total gland is not made on the same basis, since in the non-hyperplastics a very much larger proportion of the gland is removed at operation (frequently as much as  $\frac{9}{10}$ ) than is removed at operation in hyperplastic cases (rarely more than  $\frac{2}{3}$ ).

Thus, it is probable that the total amount of iodine in the entire gland in the cases of hyperplastic goitre with very advanced regression averages more than the total amount of iodine in the entire gland in the non-hyperplastic cases.

The averages of the total iodine of patients grouped as to age by half-decades shows no order or regularity, but a similar grouping of the average total amounts of iodine arranged by duration of goitre in half-decades results as follows:

#### ADDENDUM TO TABLE VII.—TOTAL IODINE AND DURATION OF GOITRE.

Duration of goitre in half-decades.	Non-hyperplastic toxic.		Non-hyperplastic atoxic.	
	Number of cases.	Average total iodine, mgs.	Number of cases.	Average total iodine, mgs.
5 -	30	19.6	23	13.7
5 +	21	18.1	37	12.3
10 +	26	21.3	28	16.9
15 +	23	32.9	30	16.9
20 +	22	28.3	20	22.5
25 +	19	22.3	11	14.0
30 +	12	22.1	1	13.5
35 +	8	28.3	2	16.2
40 +	11	28.3	3	16.0

## GOITRES, CORRELATION OF PATHOLOGICAL, CLINICAL AND CHEMICAL DATA

TABLE VII.—TOTAL IODIN IN PORTION OF GLAND REMOVED (IN MILLIGRAMS).

PATHOLOGICAL CLASSIFICATION.	
CLINICAL CLASSIFICATION.	
1. Hyperplastic toxic ("exophthalmic" goitre).	Totals (averages).
2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	
3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	
4. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	
5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).

# 1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:

- A. Early hypertrophy and hyperplasia  
B. Advanced hyperplasia  
C 1. Early regression of hyperplasia  
C 2. Advanced regression of hyperplasia  
C 3. Very advanced regression of hyperplasia

## 2. PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:

- | OF EPITHELIUM.  |     |
|---|-----|
| D. Secondary regeneration of epithelium . . . . .                     | 100 |
| H. Diffuse atrophy of epithelium . . . . .                            | 100 |
| H + F. Diffuse atrophy of epithelium with included adenomas . . . . . | 100 |

### 3. ENCAPSULATED ADENOMAS:

E, F, G . . . .

## 4. CARCINOMAS . . . . .

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Totals (averages)



While there are considerable fluctuations in the total amount of iodine present at the different half-decades, the most constant relationship is that at each half-decade the total amount in the toxic cases is materially more than is the total amount in the atoxic cases.

*Table VIII.* The determination of the  $\alpha$ -iodine has been made in too few cases to make the average percentages of much comparative value, there being but 30 cases in the hyperplastic group and 28 in the non-hyperplastic group. It may, however, be noted that in those groups in which a sufficient number of cases exist for comparison, that the following order is presented: In the cases of advanced hyperplasia, the percentage of the total iodine in the  $\alpha$  form is 16 (11 cases), and rises to 35 (18 cases) in the advanced regressions. In the non-hyperplastic cases, if the two groups with toxic symptoms are placed together (11 cases), the average percentage of the total iodine in the  $\alpha$  form is 30, while in the atoxic group (16 cases) the average percentage is 34. Thus it will be seen that there is a parallel relationship in the two groups, though until further data is obtained no great significance can be attached to it.

GENERAL DISCUSSION. 1. The data herein presented furnishes additional proof of the statements previously made by one of us,<sup>3</sup> that the symptom complex, which is generally recognized as "typical Graves's disease," "exophthalmic goitre," etc., and sharply denoted by Plummer as hyperplastic toxic goitre is constantly parallel in all its stages of development and regression with similar stages of development and regression in the parenchyma of the thyroid. This parallelism is shown in the average duration of goitre, the average duration of toxic symptoms, and in the progressive and regressive histological changes.

Now, for the first time in detail the percentages and total amounts of iodine, the pathological groups, and the clinical types have been compared in the same series of cases. As previously suggested by the work of Smith and Broders,<sup>15</sup> a close parallelism obtains throughout the data from the three sources.

From previous investigations there seemed to be little doubt that the clinical picture of exophthalmic goitre is produced, either directly or indirectly, by hyperactivity of the thyroid; but until some definite substance had been isolated from the normal thyroid and from the pathological glands and shown to be toxic in its nature, no final conclusion could be arrived at. The isolation in pure form of a compound containing 60 per cent. of iodine<sup>12 13 14</sup> and the proof that this substance is highly toxic in nature, emphasized the importance of an investigation concerning the amount and nature of the iodine-containing compounds of the thyroid. It has been shown that the iodine in the glands exists in two independent forms of combination, only one of which, the  $\alpha$  form, is toxic. We must therefore enlarge our conception of the physiological action of the iodine compounds

to include the action of this one the toxicity of which is vastly greater than that of any other hitherto described.

It is significant to find that this  $\alpha$ -iodin compound is present in the actively hyperplastic glands of advanced hyperplastic toxic goitres in only  $\frac{1}{20}$  to  $\frac{1}{15}$  the amount in which it is present in normal thyroids. This must be interpreted not as a reduced production of the toxic substance but as the result of its greatly increased diffusion from the gland into the blood stream. There is no quantitative measure of the secretory activity of the thyroid, but its storage capacity for the toxic substance is obviously proportional to its iodine content. If further observations support the relatively few herein recorded, it would seem to be a fair assumption that the  $\alpha$ -iodine compound is responsible for the toxic symptoms in hyperplastic toxic goitre. The constant direct relationship between the clinical symptoms and pathological picture and the reservoir capacity of the thyroid in hyperplastic toxic goitre is strikingly shown in Tables VI, VII, and VIII. The failure on the part of other pathologists to recognize this constant association, we believe, has been due (1) to failure by clinicians to distinguish sharply between hyperplastic toxic goitre ("typical acute exophthalmic," "Graves's disease," etc.) and the several indeterminate groups of non-hyperplastic toxic goitre ("atypical chronic Graves's disease," "cardiovascular goitre," etc.), and (2) failure to recognize the fact long ago suggested,<sup>3</sup> that the chemical constituents found in the thyroid are only the complement of those which must have gone out of the gland to have caused symptoms.

2. The relationships of the pathology and chemistry of non-hyperplastic thyroids to the various clinical groups of toxic and atoxic non-hyperplastic goitre are still far from being cleared up. This is due (1) to the difficulty in accurately grouping these cases clinically, (2) to the difficulty in securing accurate information as to the onset and course of the chronic symptoms, and (3) to the difficulty in interpreting long past primary pathological changes in the light of present pathological and chemical findings since most of these patients seek surgical aid many years after the beginning of the goitre, and probably also several years after the beginning of symptoms. That the relationship of the histological changes in the thyroids designated as epithelial regenerations is parallel with the iodine content of the glands, and to some extent with the clinical history of the patients from whom the glands were removed, is shown in the several tables.

One fact running through all the tables is that the amount of iodine in the gland parallels the clinical grouping. In the actively hyperplastic glands (group B) it has been shown that the amounts of iodine and  $\alpha$ -iodine are very low, but in cases where regression has occurred (group C) the amounts of iodine are high. In contrast to this it was found that the amount of iodine in the non-hyperplastic toxic glands is higher than in the non-hyperplastic atoxic glands.

The clinical picture, in its most severe type, of patients with non-hyperplastic toxic goitre approaches in many respects the picture of patients with hyperplastic toxic goitre. Assuming the same toxic substance to be the cause for all thyroid intoxication, the factors involved to produce varying clinical pictures, are the daily amount of absorption of the toxic substance, the length of time during which this intoxication occurs, and the personal resistance of the patient. At present we have no conclusive evidence explaining the higher iodine content of toxic non-hyperplastic glands than that of the actively toxic hyperplastic glands, but it seems probable that the diffusibility from the gland of the  $\alpha$ -iodine compound may be an important factor in determining whether a goitre produces toxic symptoms or not.

Further rearrangements of the clinical groups of non-hyperplastic goitre are in progress by Plummer, and further studies of the pathology and chemistry of the thyroids from these cases are now being made by us and will be reported later.

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## STUDIES ON THE URIC ACID IN THE BLOOD IN GOUT. SECOND PAPER.

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It is now known that uric acid is constantly present in demonstrable amounts in the blood of man. In 38 patients at the Boston Psychopathic Hospital, Folin and Denis<sup>1</sup> found that the amount of uric acid in the blood determined by their newly discovered colorimetric method varied from 0.7 to 3.7 mgs. of uric acid per 100 grams of blood. Adler and Ragle<sup>2</sup> recently reported the findings in 156 patients examined in the same hospital. The uric acid ranged from 0.7 mgs. to 4.5 mgs. per 100 grams of blood. In 107 out of the 156 cases the amount was between 1 and 2 mgs. In 11 cases there was less than 1 mg. and in 38 cases more than 2 mgs. These cases in both series were unselected. The blood was obtained from newly admitted patients taken seriatim and doubtless included somatic diseases, especially chronic interstitial nephritis, arteriosclerosis, and alcoholism. When classified according to the psychiatric diagnosis, the slight variation in the average amount of uric acid found in each group is striking. The lowest average amount was 1.31 mgs. found in 6 cases of general paresis, the highest, 1.86 mgs. in epileptic insanity, of which disease, however, there was only one case. Adler and Ragle concluded that the blood of insane patients contained the normal amount of uric acid on an ordinary diet. This is probably correct. They are the only figures based on a large number of analyses available for forming even an approximation of the variations in the amount of uric acid that is present in the blood of healthy individuals on an ordinary diet.

The view was held until recently that uric acid was not demonstrable in the blood of normal individuals on a purin-free diet. Its constant occurrence with the patient on this diet was regarded as a characteristic feature of gout, and diagnostically important.<sup>3</sup>

McLester,<sup>4</sup> using Folin's method,<sup>5</sup> found uric acid in the blood of fifteen normal individuals who had been on a purin-free diet, for at least three days, in amounts ranging from 0.5 to 2.9 mgs. per 100 grams of blood. A study of his table shows that the average amount was 1.4, while the figures given by Adler and Ragle show that the average amount in their 156 cases was 1.7. That these amounts so nearly agree, deserves to be emphasized, especially as nearly all the individuals studied by McLester were young, healthy adults on a purin-free diet, while the patients studied by Adler and Ragle were of all ages and on a mixed diet.

Very different from these figures are those obtained in gout. In 1913 I reported 11 cases of typical gout in which the uric acid in the blood had been determined by the method of Folin and Denis in Folin's laboratory.<sup>6</sup> At the present time the number of cases studied has been increased to 16. The analyses during the past two years were made by Mr. Ragle and myself in the laboratory of the Psychopathic Hospital. Only those cases are included (1) in which tophi were found; (2) in which a history of characteristic attacks of acute gout was obtained; or (3) in which typical symptoms developed while under observation.

The average amount of uric acid irrespective of the diet or the condition of the patient at the time of the examination was 3.7 mgs. Three of the patients seen during attacks were on an ordinary mixed diet. They had 4.5 mgs., 4.8 mgs., and 5.7 mgs. of uric acid. In the blood of two other patients examined during an attack while on a purin-free diet the uric acid in four determinations ranged from 2.4 to 5.1 mgs., with an average amount of 3.6 mgs. None of these patients was taking atophan.

Seven patients were examined at a time when they were free from symptoms of gout and when they were on a mixed diet. Their blood contained from 3.1 mgs. to 5.5 mgs. The average was 4.3 mgs. In the blood of six patients on a purin-free diet examined at a time when they had no acute manifestations of gout the uric acid ranged from 1.6 to 7.2 mgs., with an average of 3 mgs. These figures show that in the cases studied there was more uric acid in the blood when on a mixed diet both in the interval and during attacks than when on a purin-free diet. In all twelve examinations were made when a mixed diet was taken during attacks as well as in the intervals, and the average amount of uric acid was 4.3 mgs. Adler and Ragle, as already stated, obtained an average amount of 1.7 mg. in their 156 unselected psychiatric cases on a mixed diet. A comparison of these two figures shows that there is usually in gout a marked hyperuricemia. In the cases examined there was more than twice as much uric acid on the average than in the blood of non-gouty cases. The same conclusion is reached by taking all the analyses upon which this study is based without regard to the diet, medicines taken, or the condition of the patient at the time of the examination. Thirty-eight determinations were made on sixteen cases of gout, and the average amount of uric acid was 3.7 mgs. per 100 grams of blood.

On a purin-free diet the average amount was larger during an attack than during the interval—in the former 4.3 mgs., in the latter 2.4 mgs. The number of cases is too small to warrant the conclusion that in gout there is usually more uric acid present in the blood during an attack than at other times. That this is the rule, however, is at least suggested by the analysis of all the cases without regard to diet, whether ordinary or purin-free. Eight determina-

tions were made on six patients during an attack, and the average amount of uric acid was 4.6 mgs. Eighteen estimations were made on twelve cases when free from acute symptoms of gout, and 3.3 mg. was the average concentration.

Although these analyses and those of other investigators show that the blood in gout usually contains a relatively large amount of uric acid, the diagnosis of gout cannot be based solely on this finding, as a high concentration is sometimes found in other joint conditions; but in these the hyperuricemia has been transitory, while in gout it is usually constant. In a case of infectious arthritis which did not have the clinical features of gout, the uric acid in the blood at the first examination was 7.6 mgs. The analysis was made by Dr. Denis. Seven months later the blood was again analyzed and only 0.8 mg. was found, although the patient at the time was on a diet rich in purins. Other similar cases have shown the value of repeated blood examinations.

In typical gout the uric acid may be low at times, even when atophan has not been taken. In one of my patients the first analysis showed only 1.7 mg. of uric acid (purin-free diet), and in the blood of another case on a mixed diet there was 1.9 mg.

In the sixteen cases of gout studied no relation could be traced between the amount of uric acid in the blood and the severity or character of the disease. Two of the patients had many large deposits of sodium urate beneath the skin in different parts of the body. The blood of both contained less than the average amount of uric acid found in gout—one had 2.4 mgs. on a purin-free diet, the other 2.2 mgs. These findings show that the presence of many tophi is no indication that hyperuricemia exists.

The amount of uric acid in the blood bears no apparent relation to the age of the patient.

A considerable variation in the uric acid content may be found in the blood of the same individual within a short time which cannot be attributed to purin in the food. In my first paper I called attention to this fact. A patient admitted in a severe attack of gout had only 2.7 mgs. of uric acid in his blood at the first examination made only twenty-four hours after the purin-free diet was begun. Later the blood contained 5.1 mgs., and he had been fed no food containing purins for fifteen days.

It is not known whether or not the uric acid concentration varies considerably in healthy individuals on a purin-free diet, as sufficient observations on this point are lacking. McLester made four examinations on one healthy person who was on a purin-free diet, and the amount of uric acid was practically constant. But in some cases of gout the variation in the blood at different times may be slight. I examined one case in which the amount of uric acid was unusually low—there was 1.7 mg. present. Nearly two years later a second examination was made and 1.3 mg. found.

That two of the lowest amounts of uric acid yet recorded in gout, both well within the limits of normal, with a long interval between the tests, were obtained from the same patient indicates that the concentration of uric acid in the blood of gout may in some cases be fairly constant.

On the other hand, individuals who have no symptoms or signs of gout may have a wide variation in the uric acid content of the blood. For example, M., a patient with recurrent iritis, had 2.2 mgs. after having been on a purin-free diet for two days. A few months later when on a mixed diet his blood contained only 0.8 mg.

Great fluctuations in the amount of uric acid independent of diet are sometimes observed. This was strikingly shown in a case of primary polyarthritis. (See Table I.)

TABLE I

		Mgs. of uric acid per 100 grams of blood.
McC., aged twenty-two years.		
October.	Ordinary diet	2.7
December.	Purin-free diet	5.0
May.	Purin-free diet	1.6

In another case of chronic non-gouty arthritis the blood at the time of the first analysis contained 7.6 mgs. of uric acid. A few months later when on a diet rich in purins only 0.8 mg. was found.

After feeding five gouty patients a meal rich in purins I have observed a marked rise in the uric acid content of the blood above the upper limit of normal. (See Table II.)

TABLE II

	Mgs. of uric acid in 100 gms. of blood.		Mgs. of uric acid in 100 gms. of blood.
D. N. Gout. Purin-free diet	3.1	52 hours after eating 280 gms. haddock roe	5.8
		3 days after eating 300 gms. roast beef	6.2
K. Gout. Purin-free diet	2.1	24 hours after eating 270 gms. roast beef	3.0
H. Gout. Purin-free diet	1.7	3 days after eating 150 gms. thymus	3.6
P. Gout. Purin-free diet	2.1	3 days after eating 160 gms. thymus	3.4
J. N. Gout. Purin-free diet	2.2	48 hours after eating 190 gms. thymus	8.7
Average	2.2	Average	5.1

In four cases of gout in which the uric acid concentration at the first examination was below the upper limit of normal, 2.5 mgs., the blood after this test meal contained a large amount of uric acid.

In the investigation of my first two cases I fed roast beef, but

subsequently used sweetbreads for the purin test meal. The patients were placed on a purin-free diet for several days and then a meal of sweetbreads was given. The amount taken ranged from 150 to 300 grams (raw weight). If the patient did not eat the amount ordered at one meal the remainder was given at the following meal. After feeding the sweetbreads the purin-free diet was resumed. The blood was examined after intervals of time ranging in different cases from twenty-four hours to four days. In the three cases of gout tested there was a striking increase in the amount of uric acid in the blood one to three days after the sweetbread meal. In one case after feeding 190 grams of thymus gland the amount of uric acid in the blood was doubled in the first twenty-four hours, rising from 2.2 mgs. to 4.4 mgs. On the third day it reached a maximum of 8.7 mgs. On the fourth day it fell to 2.7 mgs.

This marked disturbance in the uric acid metabolism was not indicated by any apparent delay or diminution in the output of the exogenous purin in the urine; 26.2 per cent. of the ingested purin nitrogen was excreted as uric acid. Burian and Schur<sup>7</sup> found in a normal individual only 25 per cent. of the purin nitrogen of calves' thymus excreted in the urine as uric acid, while a healthy man studied by Pollak put out as uric acid only 15 per cent. of the exogenous purin nitrogen. In the case just cited if the increased output of uric acid comes from the purin bases contained in the sweetbreads then 26.2 per cent. of the ingested purin nitrogen was excreted as uric acid, and this is more than Burian and Schur<sup>7</sup> obtained in a normal individual. It has been demonstrated by Vogt,<sup>9</sup> Reach,<sup>10</sup> Soetbeer,<sup>11</sup> Pollak,<sup>8</sup> Mallory<sup>12</sup>, and others that in gout the excretion of exogenous purin is diminished and delayed. That this is not invariably the case was pointed out recently by Magnus Levy,<sup>13</sup> and our study of the blood shows that a marked increase and retention of uric acid in the blood may result from the ingestion of purin bases even when no evidence of retention is found on the examination of the urine.

Before diagnostic importance can be attached to this increase in the uric acid of the blood produced by the sweetbread meal in gout, the effect of feeding exogenous purins on the uric acid concentration of the blood in non-gouty individuals must be studied. The low amount of uric acid present in the blood of unselected psychiatric patients on a mixed diet (Folin and Denis, Adler and Ragle) shows that a retention of uric acid in the blood in any considerable amount for twenty-four to forty-eight hours rarely occurs; for these patients on an ordinary diet are eating purin-containing food daily, and they might take as much or more purin in their food during the forty-eight hours preceding the blood analysis as is contained in a single sweetbread meal. If the uric acid derived from this accumulated in the blood, the amount found would be considerably greater than that of individuals on a purin-



free diet. But the average amount of uric acid found by Adler and Ragle in the blood of patients on an ordinary diet was only 0.3 mg. more than that found by McLester in normal individuals on a purin-free diet.

In four non-gouty individuals the uric acid content of the blood has been determined twenty-four to forty-eight hours after feeding a sweetbread meal. The results are summarized in Table III.

TABLE III

		Mgs. of uric acid in 100 gms. of blood.			Mgs. of uric acid in 100 gms. of blood.
McC.	Chronic polyarthritis.		24 hours after eating	100	
	Purin-free diet . . .	1.7	gms. of thymus . . .		2.2
R.	Multiple recurrent throm-		48 hours after eating	300	
	bosis; streptococcus iso-		gms. of thymus . . .		2.3
	lated from blood. Purin-				
	free diet . . . . .	1.8			
M.	Chronic polyarthritis. Ord-		24 hours after eating	225	
	inary diet . . . . .	2.0	gms. of thymus . . .		1.8
H.	Chronic polyarthritis. Ord-		47 hours after eating	190	
	inary diet . . . . .	2.9	gms. of thymus . . .		2.5
Average . . . . .		2.1	Average . . . . .		2.2

On comparing the figures given in the two tables it will be seen that prior to the sweetbread meal the average amount of uric acid present in the blood of the gouty and the non-gouty patients was the same. Twenty-four hours to three days after feeding the exogenous purin the average amount of uric acid was 5.1 mgs. in the blood of the gouty, while in the blood of those who did not have gout it was only 2.2 mgs.

Exogenous purins in five gouty patients produced a marked hyperuricemia twenty-four hours to three days after they were fed, while in individuals who did not have gout the uric acid concentration was practically unchanged twenty-four to forty-eight hours after the purin meal.

These observations indicated that the uric acid derived from exogenous purin does not accumulate in the blood unless there is a disturbance in the uric acid metabolism. In one patient, however, who had recurrent iritis, but whose history and physical examination revealed no evidence of gout, the uric acid content of the blood was abnormally high two days after a sweetbread meal. His blood on November 1 after having been on a purin-free diet for two days contained 2.2 mgs. of uric acid. On November 7 he ate 150 grams of sweetbreads. Two days later there was 4.8 mgs. of uric acid in the blood. With the sweetbread meal he took two cocktails. It is possible that the alcohol caused a transitory disturbance of the uric acid metabolism. Pollak has shown that a retarded and

diminished excretion of exogenous purin may occur in chronic alcoholism. No persistent increase of uric acid existed in my patient as the blood examined on March 30 when on a mixed diet contained only 0.8 mg. of uric acid. This is a lower amount than has been found in any case of gout.

The increase in the uric acid content of the blood in gout after feeding a purin meal may not appear for twenty-four hours or more, and an initial fall has been observed in two cases of gout in which the blood was examined four to eleven hours after the sweetbread meal.

TABLE IV

D. N., aged fifty-eight years. Gout. Chronic interstitial nephritis. Purin-free diet begun March 18.

			Diet.	Mgs. of uric acid per 100 gms. of blood.
March 31.	11.30 A.M.		Purin-free	5.8
	12 noon		300 gms. roast beef	
April 1.	11.30 A.M.		Purin-free	4.6
April 2.	11.30 A.M.		Purin-free	4.5
April 3.	11.30 A.M.		Purin-free	6.2
April 4.	11.30 A.M.		Purin-free	2.8

In Case XV of my series, at 10 A.M., two hours before a sweetbread meal, the blood contained 7.2 mgs. of uric acid. At 4 P.M., four hours after taking the exogenous purin, the uric acid had dropped to 5.8 mgs. and the following morning it was 4.9 mgs. at 11 A.M. It seems remarkable that such a drop in the uric acid content of the blood should occur as a result of taking uric acid forming food into the body. The fall in this case within four hours was 1.4 mg. per 100 grams of blood. This is a considerable amount; in fact, it is equal to the average uric acid content found by McLester in fifteen healthy individuals.

This observation on the blood four hours after a purin meal was made recently, and I have not had the opportunity to repeat it on other cases of gout. In one of the first cases studied, Folin and Denis determined for me the uric acid concentration of the blood eleven hours after feeding a gouty patient, whose diet otherwise was purin-free, 280 grams of haddock roe. Only 2 mgs. of uric acid were found, while at a previous examination 3.1 mgs. were present. Two days after the roe breakfast the amount rose to 5.8 mgs. Although eggs of all kinds and caviar are included by von Noorden<sup>14</sup> in his list of purin-free foods, the output of uric acid in the urine rose 0.13 gram on the day the haddock roe was fed.

In two non-gout cases in which I have examined the blood four to five hours after the sweetbread meal, not only did this drop in the uric acid not occur, but there was a distinct increase in the amount of uric acid.

TABLE V

				Mgs. of uric acid in 100 gms. of blood.
F. Chronic primary arthritis. Purin-free diet.				
March	9.	11 A.M.		3.0
		12 noon	300 gms. sweetbreads	
		5 P.M.		3.7
McC. Chronic polyarthritis. Purin-free diet.				
February	23			2.0
March	2.	Four hours after eating 225 gms. of sweet-		
		breads		2.7
March	3			2.0

The blood of a healthy man three hours after taking an ordinary portion of chicken contained 3.9 mgs. of uric acid. Ten days later only 1.3 mgs. was present.

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## FOUR CASES OF HEMATOMYELIA: WITH A BRIEF DISCUSSION OF THE ETIOLOGY.<sup>1</sup>

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HEMATOMYELIA, or spinal hemorrhage, is a sufficiently unusual condition to justify the report of cases from a purely clinical aspect and at the same time so much variation of opinion appears to exist as to the probable causation of spinal apoplexy that additional data in regard to this aspect of the problem is definitely valuable.

It was originally designed to report the following four typical instances of hematomyelia with complete microscopic studies of the tissues, and for this purpose the spinal cords were carefully segmented and fixed. Through an unfortunate occurrence the entire collection of tissues was lost and with it the notes detailing the gross appearance of each segment. For this reason it is now only possible to discuss these cases from their clinical and etiological stand-points, but these appear to be of sufficient interest to justify the writer in presenting them.

CASE I.—Pilot, aged forty-six years. Had measles when young; malaria off and on for fifteen years. Gonorrhea sixteen, and syphilis twenty years ago.

Spasmodic drinker of beer, whisky, or anything convenient, sometimes drunk every other day. Chews and smokes. Has been always pretty well, save for several minor accidents.

*Present Illness.* Drank heavily all day, slept very well that night. Went into the saloon the next morning for a bracer. While seated in the rear room he suddenly lost himself and did not rouse until he waked in the alcoholic wards of Bellevue Hospital. Total motor and sensory paralysis below the arms, incontinence of urine and feces. Marked and increasing priapism. Paralysis ascended quite rapidly to arms.

Temperature fluctuated irregularly from 96° to 104°. Pulse rate also varied greatly, not corresponding with temperature curve but ranging from 56 to 120. Respiration entirely diaphragmatic, from 12 to 26, without reference to temperature or pulse. Pulmonary and cardiac status practically normal.

Complete loss of sensation, of temperature, pain, and touch, with complete motor paralysis below level of third dorsal nerves. Patellar, cremasteric, abdominal, and wrist reflexes entirely lost. Incontinence of feces and retention of urine.

After a few days there was some regain of sensation and power in the arms and shoulders. Mentally he became perfectly clear.

<sup>1</sup> Read by title before the meeting of the Association of American Physicians, Washington, D. C., May 11, 12, and 13, 1915.

Patient finally sank into a comatose condition and died twenty-three days after the hemorrhage.

Autopsied by permission and on the assurance that only the spinal cord would be examined. A large terminal acute and an old hemorrhage was found involving the cervical and lower dorsal segments. The hemorrhage had followed down the ventricle of the cord, infiltrating out thence into the gray matter. The columns seemed to be free from the lesion. Spinal vessels sclerosed.

CASE II.—J. C., salesman, aged sixty-seven years. Had "bilious" and typhoid fevers in 1865. One attack of gonorrhea. Syphilis denied. Two heat prostrations. Has drunk very moderately. Good and regular habits.

While driving his horse on the speedway he became suddenly dizzy, turned his cart, and collided with another vehicle. Was thrown out, landing on shoulders and head. He remained unconscious for about five minutes during which he was carried to the subway and was met by an ambulance.

Examination showed no voluntary motion below the shoulders. All reflexes below the nipple line were absent. Sensation markedly decreased above this zone. Touch perception present but markedly dulled along the ulnar distribution on both arms. Sensation of heat and cold lost. The paralysis is perfectly symmetrical. There is a small contusion over the sacrum but none elsewhere.

Respiration is entirely diaphragmatic; thorax does not move at all. Forced respiration extends to sternocleidoid and scaleni muscles. Temperature,  $98.4^{\circ}$ ; pulse, 80; respiration, 24. Very marked continuous priapism.

On the second day the patient developed first a posterior congestion of the base of both lungs succeeded by pneumonic consolidation. Urine and feces incontinent. The mentality became entirely normal; the priapism disappeared.

Seven days after onset the lung status had nearly cleared, but the slight contusions and abrasions of the skin failed to heal, and showed signs of trophic ulceration. Slight movement of the chest muscles became then apparent and the movements of the upper extremities became more improved and better correlated. Slight reflex, after pricking the plantar surfaces of the feet, appeared. Bowels less incontinent. Chest clearing.

Apparent improvement continued until nine days after onset, when quite suddenly the patient became very cyanotic and unconscious. Pulse slow and very feeble; pupils contracted; deviation of left eye; Cheyne-Stokes respiration; complete relaxation of muscles of the extremities; early death.

The autopsy was performed by permission a few hours after death.

The muscles of the paralyzed extremities showed the early evidences of atrophy. Except for the contusions mentioned, there was no evidences of traumatism, no fractures or evidences of

intradural hemorrhage. The arteries and veins of the spinal arachnoid showed some congestion, especially in the upper cervical regions. They were moderately sclerosed.

There was a moderate general softening and a dilated ventricle from the medulla to the sixth cervical segment. Here the gray matter was soft and hemorrhagic and the dilated ventricle was filled with a bloody, grayish, pasty material. The seventh segment showed complete blood infiltration of the gray matter. In the eighth segment the hemorrhage was most marked and had a fresh appearance, especially in the posterior horns. In the first dorsal segment the hemorrhagic softening was very marked in the horns, mostly in the posterior, but in the lower half of the segment it was chiefly confined to the left crescent of the gray matter. In the second dorsal segment the softening was entirely confined to the left crescent, more in the posterior horn, but becoming less and less in the lower levels of the segment. The third dorsal segment showed the same changes in lesser degree, but with general congestion of the bloodvessels.

From this level down to the seventh dorsal there was very little disease, but here the ventricle and its adjacent tissue showed a hemorrhagic softening. The eighth segment showed a simple dilated ventricle without hemorrhage. Blood again appeared in the ventricle at the level of the tenth dorsal segment with the usual extravasation outward. A small psammoma was found attached to the posterior root, on right side, just as it was given off from the cord.

There was a small hemorrhagic area in the left posterior horn of the second lumbar segment; another such area was found located near the ventricle. The third lumbar segment showed a very similar condition. The same was found in the fourth lumbar segment, but the sacral levels showed no changes aside from a general congestion. The cauda showed no gross disease.

The brain showed practically nothing except for isolated patches of slight arachnoid thickening and congested and sclerosed bloodvessels. No hemorrhagic foci were found on gross examination. The arteriosclerosis, which is evidently of long standing, showed moderate calcareous changes.

The basal ganglia showed nothing, and careful sectioning of the pons, cerebellum, and medulla failed to demonstrate any gross abnormalities.

Examination of the general viscera was limited by the terms under which the autopsy was obtained. In so far as studied they showed no lesions of importance except a patchy, pneumonic consolidation, apparently resolving and a chronic interstitial with an acute parenchymatous nephritis. The general bloodvessels showed extensive sclerosis.

CASE III.—A marble cutter, married, aged forty years. Had measles when a child. Fourteen years ago had a gonorrhea. Denies lues.

Five weeks ago had an attack of vertigo which lasted about one week. Nine days ago, while at South Beach, the patient went to stool; being constipated he strained very hard. When he attempted to get up he found that he had lost control of his legs. He had burning pains from the thighs down until three days ago, since which he has experienced shooting pains but twice. His bowels have not moved, and he has to be catheterized. Patient has recently been working in a damp house; to this he attributes his trouble. He has been an inveterate user of tobacco, and has been moderately alcoholic.

He is well nourished, tongue slightly coated, appetite good, bowels constipated. Physical examination of the chest is negative. There is loss of sensation and motion below both knees. Imperfect sensation (heat, touch, pain) of lower one-third of thighs, scrotum, and arms. Cremastic and patellar reflexes, also ankle clonus, absent. Muscles of calves flabby; no priapism at present. Temperature, 98°; pulse, 90; respiration, 24. Mental status entirely normal.

Patient was put to bed, and in addition to general treatment was given daily massage of the paralyzed extremities. At the end of eight days he was moving the legs slightly, but he had developed a trophic ulcer over the sacrum. Sensation was greatly disturbed, but present in some degree even in the legs; distribution did not seem to be constant. Constipation was still very marked and drastic measures were required to induce movements. Cystitis no better.

Thirty-four days after admission he had regained control of the sphincters in large part, but atrophy of the involved extremities was steadily increasing. Cystitis and the bed-sore became progressively worse. He sank into an apparently septic condition, and died forty-one days after admission, fifty days after the acute onset.

The autopsy was performed eighteen hours after death.

Body extremely emaciated. Extreme atrophy of both legs, especially of the anterior tibial groups. No atrophy of the muscles of the upper extremities or of the thorax or abdomen.

The heart showed brown atrophy; the aorta marked endarteritis, but without calcification. Aortic and mitral segments thickened. The large vessels of the abdomen showed moderate endarteritis. Lungs showed emphysema and cavitation in the apices, apparently tuberculous, but no longer active. The liver was fatty. The kidneys showed marked chronic interstitial and fatty, with parenchymatous changes. The renal arteries showed marked endarteritis. The bladder showed ulcerative cystitis.

The second to the sixth inclusive posterior spinal processes were bifid. The vessels of the spinal canal showed extreme congestion,

especially in lower dorsal and lumbar regions. They showed moderate sclerosis. The spinal dura was normal. The first evidence of spinal disease was found at the first dorsal level, manifested by a small area of softening in the left anterior horn. At the level of the fifth dorsal segment the entire gray matter was soft and infiltrated with blood. In the mid-dorsal region the anterior horns appeared to be almost universally softened. In the lower lumbar region the softening had so generally involved all structures as to convert it into an unrecognizable mass.

The direct cause of death was sepsis originating from a large trophic ulcer over the sacrum or from the cystitis.

CASE IV.—The patient entered the fourth medical service of Bellevue Hospital unable to give any personal history, and the few details obtained were given by her neighbors.

She was twenty-five years old, supposed to be in good health, and no previous illnesses were known of. She was known among her neighbors as a hard drinker and as of liberal morals. Two days previous to her entrance to the hospital she complained of some headache. On the succeeding day she still suffered, and during the morning drank a quart of whisky. In the afternoon she felt considerably better, but at about 6 P.M., while at stool, she noticed that her feet and hands were becoming numb. She was taken to the hospital on the next day. Absolute anesthesia and paralysis of the lower extremities, abdomen, and, to a lesser degree, of the thorax also, together with slight involvement of the upper extremities. The paralysis and anesthesia rapidly extended upward, and she died before her physical examination had been completed.

The autopsy was performed early the next day, the body having meantime been preserved by efficient cold storage. The external examination of the body revealed nothing except that the pupils were irregularly dilated. The condition of the body indicated involuntary evacuations of feces and urine.

Examination of the spinal canal was only permitted. A large amount of clear colorless cerebrospinal fluid was found, and the vessels of the channel, including those of the spinal dura, were found much congested and considerably sclerosed.

Gross examination showed involvement of the spinal gray matter alone. It was found to be the seat of an acute hemorrhage, softening extending from the cervical levels downward. Apparently the hemorrhage had progressed along, and mostly, if not entirely, through the medium of the ventricle of the spinal cord.

One factor which all of these instances possess in common is that in each, definite disease of the spinal bloodvessels was present. In Cases I and IV syphilis is thus, in all probability, the chief determining factor, and in Case II age is apparently of most definite bearing, though this example also presents the only instance of a possible traumatic factor. Case III represents as the most likely



agent concerned in the production of arterial disease the excessive use of tobacco and alcoholism, which is also a factor in Cases I and IV.

These facts are in direct contraversion to the commonly accepted text-book statement. Thus Church and Peterson state that the changes in the arterial coats are of lesser importance in spinal hemorrhage, and E. Farquhar Buzzard, in Osler's *System* (vol. vii, p. 274), makes the statement that sclerotic changes in the vessels do not appear to very generally determine the lesion. The author is impressed from the statements made by most authors that cases have not been adequately investigated as to this possibility, which is of acknowledged importance in every other type of hemorrhage. It would appear to the writer that spinal hemorrhage in this characteristic in no way differs from hemorrhage elsewhere, and that it is especially similar to brain hemorrhage.

The statement is made by some authors that spinal hemorrhage customarily takes place in a previously existing area of softening. Though it is impossible to absolutely exclude this possibility, at least it seems highly improbable, for in the cases thus reported any lesion of sufficient size to favor such a condition could not long exist in so limited and vital a territory as the spinal cord without producing symptoms of an obvious character. Such signs are entirely wanting in these cases. Eichorst, in 1874, recognized that central hemorrhage might take place in previously normal cords, and in all probability this is the rule and not the exception.

As to the immediate determining factor, Buzzard states the most frequent to be trauma or strain, and Church and Peterson seem impressed with the idea that arterial pressure and direct cardiac impulse which play so important a role in brain hemorrhage are absent or unimportant matters in spinal hemorrhage. The writer's impressions from a study of the literature of the subject and from these 4 cases is that precisely similar factors are at work here as in cerebral hemorrhage, but obviously under conditions varying from those dominant in cerebral hemorrhage. Thus, for example, we find cerebral hemorrhage occurring most frequently in conditions of mental strain, and in all except Case II of this group a definite factor of primary spinal stress was present. Straining at stool was apparently the immediate cause in two of my cases. Oppenheim cites a case occurring during the manual of arms drill. Gowers mentions a case occurring after excessive coitus, and so on.

Traumatism is mentioned by most authors as an important factor in the cause of spinal hemorrhage. One should exclude in this discussion those instances in which actual crushing of the cord occurs, since the lesion in true hematomyelia is one of gray matter hemorrhage only and is quite distinct from that which might occur in direct spinal injuries. In only one of these four instances is a possible traumatic factor concerned, that is in Case II. It must,

however, be noted that no evidence of direct spinal injury was found postmortem in even this instance, and it is possible that the hemorrhage caused the fall, resulting in the accident, and not *vice versa*.

As is always the case in hematomyelia, the blood extravasation has extended along and about the spinal ventricle, and in no instance has extended out into the white matter. This is doubtless due, as all students of the subject have conceded, to purely mechanical factors.

In conclusion, as a result of the study of these instances, one is impelled to the idea that contrary to the prevailing view, arterial changes as a predisposing factor are present in hematomyelia, and that the dominant agent in the immediate determination of the hemorrhage is that of strain, involving spinal activity or tension.

## THE USE OF THE DUODENAL CATHETER IN DIAGNOSIS.<sup>1</sup>

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AFTER the first attempts to catheterize the duodenum, many years ago, by Hemmeter<sup>2</sup> and Kuhn,<sup>3</sup> this procedure was looked upon purely as a scientific curiosity, principally because of the cumbersome instruments used, until 1910, when Einhorn<sup>4</sup> and Gross<sup>5</sup> each devised a simple rubber tube, with a metal tip, which they managed to get past the pylorus with more or less ease. After the introduction of these improved instruments it was found by Einhorn<sup>6</sup> that they could be used satisfactorily in the treatment of several diseases, notably gastric and duodenal ulcers, gastritis, and pylorospasm. Einhorn and others have since found it of value, also, in the treatment of certain other troubles of the gastro-intestinal tract, such as the toxic vomiting of pregnancy,<sup>7</sup> duodenitis, etc. Recently, moreover, Einhorn<sup>8</sup> reports favorable results in cases

<sup>1</sup> From the Medical Department of the University of Texas School of Medicine.

<sup>2</sup> Arch. f. Verdauungskr., Band ii.

<sup>3</sup> Ibid., Band iii.

<sup>4</sup> Jour. Amer. Med. Assoc., 1910; Berl. klin. Woch., 1910, Nos. 12 and 34; Arch. f. Verdauungskr., Band xviii; Ibid., Band xix.

<sup>5</sup> Münch. med. Woch., 1910; Wien. klin. Woch., 1910; Arch. f. Verdauungskr., 1914, xx, 338.

<sup>6</sup> Loc. cit.

<sup>7</sup> Morgan, AMER. JOUR. MED. SCI., 1914, cxlviii; Carroll, Maryland Med. Jour. 1913, iv, 243; Hess, loc cit; Palefski, Interstate Med. Jour., 1914, xxi, 997; Reuss, Berl. klin. Woch., 1914, li, 1023; Hess, Verhandlung der Gesell. f. Kinderheilkunde, 1913.

<sup>8</sup> Loc. cit.

of cirrhosis of the liver and cardiac decompensation, where it is desired to give an irritable stomach a complete rest.

Except as a means of treating these diseases, the duodenal tube has been regarded until quite recently as an instrument of comparatively little diagnostic value. It has facilitated the study of the pancreatic secretions, the bile, the flora of the duodenum,<sup>9</sup> etc., but has not been of any great diagnostic importance except, occasionally, in a case of advanced pancreatitis, perhaps, or in complete obstruction of the ampulla of Vater from new growths, gall-stones, etc. (Einhorn, Chase<sup>10</sup>).

Quite recently, however, some rather interesting observations on the use of the duodenal tube in diagnosis have been made. Chase<sup>11</sup> has reported a study of the pancreatic ferments in a number of cases, including a few of pancreatitis. Einhorn<sup>12</sup> reported recently some observations of the bile in gall-stone disease, in which he concludes that a turbidity of this fluid is of some significance in diagnosing such conditions. He also believes that the continued absence of any one of the pancreatic ferments is significant in the diagnosis of pancreatitis. Einhorn noted, also, an increased amount of mucus in the duodenum in certain cases of duodenitis, and believes this to be of some value in the diagnosis of that condition. Crohn<sup>13</sup> has recently published a report of several interesting cases of new growths about the head of the pancreas in which the absence of the pancreatic ferments was an important factor in the diagnosis. Bondi and Salomon,<sup>14</sup> of von Noorden's Clinic, have reported several cases of achylia pancreatica diagnosed by means of this tube, and Bondi<sup>15</sup> has also reported a thorough and complete study of the duodenal contents, both microscopically and chemically, in a great number of conditions. Bondi's observations are of such interest, and bear so closely on the work which we are about to report, that perhaps a few words regarding his findings will not be superfluous. His report is based upon the chemical and microscopic analyses of 200 duodenal contents, coming from 153 different individuals. He concludes, as a result of this experience, that such an analysis is of considerable diagnostic importance in certain diseases. In one case of cholecystitis, for instance, he was able to confirm the diagnosis from the presence of innumerable bile-stained pus cells in the duodenal contents. In one case of acute duodenal ulcer the presence of blood and pus cells gave some rather definite information as the local trouble. In certain systemic diseases, moreover, associated with considerable blood destruction, he was able to demonstrate a decided increase in the urobilin content

<sup>9</sup> McNeal, *Arch. Int. Med.*, 1913, xxi, 178; Hess, *Jour. Infect. Dis.*, 1912, xi, 71.

<sup>10</sup> Einhorn, *loc. cit.*; Chase, *Arch. Int. Med.*, vol. xii.

<sup>11</sup> *Ibid.*

<sup>12</sup> *AMER. JOUR. MED. SCI.*, 1914, cxlvii, 490.

<sup>13</sup> *Ibid.*, 1914, cxlviii, S39.

<sup>14</sup> *Wien. med. Woch.*, 1913, lxxiii 1722.

<sup>15</sup> *Arch. f. Verdauungskr.*, Band xix.

of the bile removed by means of this tube. His results were disappointing in a number of cases of ulcer of the stomach and duodenum, however, the contents being apparently quite normal.

Bearing in mind the above-mentioned researches, and believing that there is still a remarkably fertile field for research along these lines, we feel that the report of certain investigations in which we have been engaged for the past eighteen months would not be out of place.

Our technique in making these examinations has differed rather materially from that ordinarily employed. In the first place we have found that a careful microscopic study of the empty stomach contents, with particular attention paid to the cellular elements, will, in many cases, give definite information as to the condition. This is true, also, of the microscopic examination of the duodenal contents. The recent interesting reports of Loeper and Binet,<sup>16</sup> and of Simon<sup>17</sup> and Chaussade,<sup>18</sup> in France, on this subject, have stimulated our belief in the efficacy of direct microscopic study of the stomach contents materially, and while we believe that these authors are perhaps somewhat optimistic in their conclusions, nevertheless we believe that important information is often overlooked by the neglect of such a study. For this reason we have, since the inception of this work, in our endeavor to obtain the gastric and duodenal secretions in a natural state, and unaffected by any artificial means, carefully avoided the administration of tea, as recommended by Einhorn in the passage of this tube, or of water, etc., as recommended by others. Observing this precaution, and given a perfectly empty stomach, we are able to obtain a pure secretion in practically every case. The results which we have obtained from such a study we shall take up in detail in this paper. We have, moreover, found a modification of the Einhorn tube, the so-called Jutte duodenal tube, to be superior to any other duodenal catheter which we have tried for our purposes. We prefer this tube for two reasons: In the first place the tip is practically of the same diameter as the tube, allowing a more rapid passage of the pylorus. In the second place the tube is provided with a stiff wire, enabling one to pass the tube through even an acutely irritable pharynx with little or no difficulty. The wire can be easily withdrawn as soon as the pharynx is passed. With these two exceptions we pass the tube in the usual manner. Contrary to the opinion of some (Palefski<sup>19</sup>), we believe that the passage of this tube is an extremely simple procedure, and that it can be readily passed in the usual case by any physician of moderate intelligence. We find that a small rubber aspirating bulb facilitates the removal of the secretions considerably.

<sup>16</sup> Arch. d. mal. de l'app. digest., 1914, viii, 181.

<sup>17</sup> Press Méd., 1914, xxii, 265.

<sup>18</sup> Rev. de Méd., 1914, No. 6.

<sup>19</sup> Loc. cit.

Our examinations of the contents removed have consisted in the following steps:

1. Gross appearance: color, amount, mucus, blood, etc.
2. Microscopic: pus and blood cells, gastric epithelial cells, amount of mucus, bacteria. In the duodenal contents all bile-stained cells should be carefully studied.
3. Chemical: free HCl, total acidity, lactic acid, Wolff-Junghan's test for dissolved albumin, pancreatic ferments.

Perhaps it would be well to state that two requisites must be observed before one draws any conclusions from such a study as that above outlined. One must, in the first place, be perfectly familiar with the microscopic appearance of the contents from the normal empty stomach and duodenum. This is more easily said than done, and can be accomplished only after the study of a number of normal cases. The chief difficulty with which one has to contend at first is that of differentiating in the gastric contents, the true gastric epithelial cells from pus cells, alveolar cells from the lungs, epithelial cells from the mouth, pharynx, and esophagus; and, in the duodenal contents, one must, of course, recognize the cells which have come from the stomach. We are satisfied, however, that with a sufficient amount of experience the important cells in both gastric and duodenal contents can be recognized with little difficulty. The next requisite which must be observed is the prompt examination of the secretions as soon as they are removed, and before the important cells have lost their characteristic appearance from digestion. The examination is best made in the fresh state, using first low and then high power, in the same manner as one ordinarily examines urine for casts.

Our findings with the above technique have been encouraging. In some 25 normal cases we have found rather constant pictures. The free HCl ranged from 0 to 30, the total acidity from a trace to 30, the total acidity usually varying only a few points from the free HCl reading. We have found a fairly constant amount of mucus in the normal stomach contents, usually consisting of white strands floating in the secretion, and containing always numerous polymorphonuclear cells. It must be borne in mind that the appearance of many leukocytes enclosed in this mucus is normal. It is only those leukocytes which are floating free in the secretion which are of significance. A few oval or cylindrical gastric epithelial cells are also often found, but such cells are never very numerous. Our observations in this regard have agreed with those of Chaussade and of Loeper and Binet, to whose excellent studies of the cytology of the empty stomach in normal and morbid conditions the reader is referred for further details.<sup>20</sup> As for the Wolff-Junghan's<sup>21</sup> test

<sup>20</sup> Chaussade, loc. cit.

<sup>21</sup> Berl. klin. Woch., 1911; Med. Klin., 1912; Smithies, AMER. JOUR. MED. SCI., 1914, cxlvii, 713; Rolph, Med. Rec., 1913.

of the empty stomach contents under normal conditions, we find that the percentage of dissolved albumin is fairly constant, the ring appearing practically always in either the second or third tube, rarely in the fourth. The duodenal tube passes the pylorus in the great majority of these cases in from ten to fifteen minutes after its introduction.

The microscopic study of the normal duodenal contents is simple. The fluid is clear, bile-stained, seromucous, and contains few cells except for the partly digested gastric cells, which have already been noted. The Wolff-Junghan's test of this secretion usually gives an albumin ring in the third tube, occasionally in the fourth, but, in our experience, never in the fifth or sixth tube normally. So far as I am aware there are no previous reports as to the application of the Wolf-Junghan's test to the duodenal contents. Brauer<sup>22</sup> has shown that the bile of the normal dog is albumin-free, but that albumin appears in it after the administration of phosphorus, alcohol, etc., in toxic doses, so that, apparently, the presence of albumin in this fluid is a sign of damage to the liver. Unfortunately, however, we have three other albumin-containing secretions to deal with before we can draw any definite conclusions as to the increase of albumin in the duodenal contents. Fortunately we can control the albumin content of the stomach by direct examination, and when there is a material difference between the readings of the gastric and duodenal secretions in this regard, we know that the increase must come either from the bile, from the pancreatic secretion, or from the secretion of the duodenum itself. Only extensive experience will show whether such a test is of material value, but several observations which we have made have at least been interesting to us. The three pancreatic ferments we have found to be present constantly in normal cases.<sup>23</sup>

Our series of studies on pathological conditions of the gastrointestinal tract consists of observations on some 60 selected cases, which we shall take up in detail. The most common condition studied in our series has been chronic gastritis. We have 12 cases of this condition, in which the findings were fairly constant and were as follows: The secretion is usually obtained from the stomach with some little difficulty, being often tenacious from an excess of mucus. (Occasionally it becomes necessary to inject several hundred centimeters of water, preferably normal saline, before a sufficient amount can be obtained. This is exceptional, however.) There is usually no free HCl. The reaction is apt to be neutral, or, at least, very faintly acid. Occasionally, however, both the free HCl and the total acidity are fairly high. Micro-

<sup>22</sup> Zeit. f. Physiol. Chemie, Band xl.

<sup>23</sup> These tests have been carried out in the usual manner: that of Wohlgemuth for diastase; of Gross for trypsin, and the method described by Bondi, for lipase (loc. cit.)

scopically, one sees numerous well-preserved pus cells floating free of mucus. A few flecks of blood may be observed in the mucus. In the very old chronic cases, gastric epithelial cells are usually very scarce, if not absent. In a few cases, however, they have been more numerous than normal. Considerable difficulty is usually experienced in these conditions, in getting the tip of the duodenal tube past the pylorus, apparently due to a lack of gastric motility. In two of this series it was necessary to leave the tube *in situ* over night before the duodenal contents could be obtained. A typical picture of this condition would therefore be, in our experience, an excess of mucus, causing a thick, tenacious secretion, few cellular elements (except pus cells), and a sluggish motility, with no free HCl and a low total acidity.

The cases of acute and subacute gastritis, which we have studied, of which there were four, have differed from this picture in several respects. In the first place, there was usually a fairly high percentage of free HCl, as well as a higher total acidity. There is not usually so much mucus. In all of our cases the cellular elements were materially increased, especially the gastric epithelial cells, which often appeared in showers, as it were, being numerous in one specimen examined and not so numerous in the next. They were always increased, however. The pylorus was passed with little difficulty in three cases. In the fourth considerable difficulty was experienced. It may be well to state here that our diagnoses, both of the acute and the chronic gastritis, were made from the ordinary clinical and laboratory examinations, and not by means of this study. A fairly large percentage of them were operated upon for other conditions, at which time the diagnosis was confirmed at operation (four cases). We feel, however, that this direct method of study would perhaps bring about a better classification of such conditions.

We have studied three cases of hypersecretion in this series. In all three of our cases there was a continuous watery, highly acid secretion, there being apparently no tendency for the secretion to cease so long as the tube remained in place. The free HCl in these cases varied from 60 to 80. Microscopically the gastric and duodenal contents of two were negative. There was a definite increase of the gastric cellular elements in the third case, which we believed to be a case of gastritis (from this study). One of these cases was demonstrated at operation to have no evident organic cause accounting for the trouble. Laboratory and Roentgen-ray examinations were negative in the other two. All three were strong, robust men. We believe that this method is an ideal one for the study of these cases of hypersecretion.

The study of ulcer of the stomach and duodenum in our cases has been disappointing. In acute, actively bleeding ulcers one can, of course, recognize the red blood cells, which are usually

partially hemolized. We have been able, in one case of suspected ulcer, as judged from the other laboratory tests, to say from the direct study, that it was probably a case of chronic gastritis, which diagnosis was confirmed at operation. With the exception of the bleeding above mentioned, which we have never found in the chronic or subacute cases, there is in our experience no information to be gained from such a study as we have made. We have felt, on one or two occasions, that the presence of a few red blood cells, enclosed in mucous strands, with perhaps more gastric cells than normal, would point to ulcer. In one such case in particular we felt so sure of this that we were willing to make a positive statement to that effect. The case turned out to be, at operation, a carcinoma of the cecum. The gastric cells and red blood cells certainly came from a gastritis, but I may say that the case was typical, clinically, of duodenal ulcer. With one case of syphilitic ulcer of the pylorus, however, we have had better success. In this case the appearance of numerous, free red blood cells, along with innumerable pus cells and cylindrical gastric cells, which were only noted when the tip of the tube had become engaged in the pylorus, led us to state certainly that there was an ulcerative process at the pylorus. This was confirmed at operation, which was done on the suspicion of carcinoma. This case has already been reported.<sup>24</sup>

Our study of a limited series of cases of carcinoma of the stomach, six cases, of which two were operable, has been interesting to us. In the first place, we find, as a rule, a picture at first suggesting a subacute or a chronic gastritis, both from the gross and from the microscopic appearance. As for the finding of cells showing malignant changes (mitoses, etc.), upon which some writers lay such stress,<sup>25</sup> we have been rather unsuccessful,<sup>26</sup> perhaps because we are not sufficiently trained in the proper technique, but certainly we are unable to substantiate their claims as the great value of these cells in diagnosis. We find, however, in addition to the signs of a gastritis in these cases, a rather interesting chemical change. In all of our cases free HCl was entirely absent from the content of the empty stomach, and the total acidity, instead of remaining low, as in chronic gastritis, was in all of our series except one comparatively high, ranging from 25 to 60. Lactic acid was, of course, present in the advanced cases only. Another interesting feature of such a study as this is the comparison of the acidity (free and combined HCl) of the empty stomach to that obtained after an ordinary test meal. This test, a modification of the well-known Glutzenski test, was suggested by Ehrenreich.<sup>27</sup> In normal cases,

<sup>24</sup> McNeil, Jour. Amer. Med. Assoc., January 30, 1915.

<sup>25</sup> Chaussade, loc. cit.; Loeper-Binet, loc. cit.

<sup>26</sup> In two cases, however, we have found cells which were very suspicious of carcinoma cells.

<sup>27</sup> Berl. klin. Woch., 1914, No. 33.



and also in gastric ulcer, the acidity rises after such a test meal. In carcinoma ventriculi, however, it remains practically stationary, or may even be lowered. In chronic gastritis it usually rises slightly, and occasionally the rise is rather marked. Two of our carcinoma cases showed a slight increase in acidity after a test meal, but none showed the material increase which is present normally. The results of the Wolff-Junghan's test, as applied to the contents of the empty stomach, in these cases showed constantly, a rather high albumin content, the readings on the empty contents being about the same as after a test meal. We have found this test either positive or suggestive in all of our series of carcinoma cases, and believe it to be of some value. We believe, however, that the positive test can be foretold in many cases from a microscopic study of the stomach contents; those cases showing many cellular elements, especially, pus cells, often having a high reading. This point deserves further study, however. The passage of the tube through the pylorus will, of course, depend upon the location of the growth. The duodenal contents were normal in these cases.

We have studied only one case of carcinoma of the head of the pancreas. In this case there was obstruction to the ampulla of Vater, and we were able to make the diagnosis from the absence of pancreatic ferments in the duodenal contents and in the stools.

We have had an opportunity to study only one case of chronic pancreatitis, of which we were sure. This case was associated with a pancreatic cyst, and showed a constant diminution in the pancreatic ferments, and usually an absence or only a trace of lipase. These tests were made both on the stools and on the duodenal contents. This case was also interesting clinically, showing a transient glycosuria, periodic attacks of abdominal pains and tenderness, inability to digest excess of fats, etc.

Three cases of achylia pancreatica were studied by means of this tube. All showed clinical signs suggesting the stomach as the seat of trouble rather than the pancreas, but pancreatic ferments were constantly absent from the duodenal contents in all three cases. In all three cases, however, diastase was demonstrated in the stools after the manner described by Brown, so that one might be justified in doubting whether these were really cases of pancreatitis.\* Such cases are certainly not normal, and undoubtedly call for further study. None of these three went to operation, so that we have no means of knowing the true condition. The stools of all three showed a certain amount of azotorrhea, and in one case this was marked.<sup>25</sup>

Our opportunities to study acute cholecystitis by this method have, unfortunately, been rather limited. Observations have been

<sup>25</sup> Since this was written one of these latter cases has come to operation, which revealed a much hardened and indurated condition at the head of the pancreas. A diagnosis of chronic pancreatitis was made by the surgeon. No other abnormalities were found.

made only on three cases. In one we were able to confirm the observation of Bondi as to the presence of bile-stained pus cells. They were not so numerous, however, as one would expect. In the other two these were not found, but in one, typhoid cholecystitis, in addition to numerous typhoid bacilli, we found numerous bile-stained cells, which we believe to have come from the epithelial linings of either the gall-bladder or some of the gall passages. The third case, a subacute one, showed nothing of note except possibly a few more cellular elements from the biliary tract than one would expect.

In four cases of atrophic cirrhosis of the liver which we have studied by means of this method, we have found several pictures which have interested us considerably. In two cases we have found quite a number of bile-stained, polymorphonuclear cells, associated always with cells which we are accustomed to call "liver cells." These cells are, in our experience, not found under normal conditions in any appreciable number. One or two, in several preparations, may perhaps be noted, but we have never found them numerous except in this condition. They are slightly larger than the normal polymorphonuclear leukocyte, are always rather deeply bile-stained, as contrasted with the cells coming from the stomach and elsewhere, have a granular, refractile protoplasm, and are round or oval in shape. There is a single, small central nucleus. Occasionally a group of these cells will be found arranged in the form of a cast. In all four of our cases such cells were fairly numerous. We were also greatly interested in the albumin content of the duodenal contents in these cases for the reason previously mentioned. Three of these cases failed to show any albumin increase by the Wolff-Junghan's test, but one case, in an early stage, showed a marked increase over the normal. An operation had been preformed on this case and a typical hob-nailed liver had been found unexpectedly. This case also showed numerous bile-stained cells, such as we have described, although no pus cells were seen.

One case showing a large tender liver, and who had also a strongly positive Wassermann reaction, showed a marked increase of albumin in the duodenal contents, although the albumin content of the stomach was normal. This case, however, showed nothing abnormal in the duodenal contents microscopically. There is also one other peculiarity about these cases which we have frequently noted, which was found likewise in our cases of gall-bladder disease: This is the presence of bile in the gastric contents removed from the empty stomach. Einhorn<sup>29</sup> has found this phenomenon to be present in several cases of gastropnoia. We have found it so far only in these cases above mentioned, and in one case which we believed to be duodenitis. The presence of a turbid bile, which Einhorn mentions,

<sup>29</sup> AMER. JOUR. MED. SCI., cxlviii, 490.

has also been noted in several of these cases, in two cases of cholecystitis and in two cases of cirrhosis. We have also found the bile turbid in several other cases, however, which have been demonstrated not to have had any gall-bladder or hepatic trouble. Three cases of chronic passive congestion of the liver have given negative results from such a study with the duodenal tube.

There is one other condition which is often mentioned, but which is seldom described, in which a study by means of this tube is of interest. This is the so-called duodenitis. Three cases which we have studied in this series have, we believe, been suffering from this trouble. All complained of pain in the right upper abdomen, suggesting in every case gall-bladder trouble. All were men, and all were past middle age. The duodenal contents in each of these cases showed a considerable amount of stringy mucus, numerous gram-negative, motile bacilli, occurring usually in strings, and numerous cocci. These bacteria were in all three cases the most prominent picture in the microscopic field. In all of these cases, also, there seemed to be more leukocytes in the duodenal contents than were found in the gastric contents, although this point may be difficult to determine, since it is merely relative. Two of these cases went to operation. Neither showed any trouble in the abdomen which could account for the symptoms of which they complained.

We have studied four cases of typhoid fever by means of this tube, three of whom were convalescent, in the hopes of discovering the presence of typhoid bacilli in the bile. This we have been able to do in three cases. We would therefore suggest, as Hess<sup>30</sup> and McNeal<sup>31</sup> have already done, that we have in this tube a valuable means of detecting typhoid carriers.

Finally, as a result of this work, which is, unfortunately, limited, but which we hope to continue, we believe that we are justified in drawing the following conclusions:

1. The direct method of study of the pure gastric and duodenal contents is of value in diagnosing certain conditions of the gastrointestinal tract, *i. e.*, acute and chronic gastritis, carcinoma ventriculi, acute ulcerations, pancreatitis, duodenitis, continuous hypersecretion, etc.

2. We feel that a further study of the hepatic and biliary diseases, along the lines which we have mentioned, would be of great interest, and we feel that, at least in certain cases of such disturbance, such studies might be of great value.

3. The absence of pancreatic ferments in the duodenal contents is a significant feature of obstruction to the pancreatic duct, and is especially valuable when associated with a marked diminution of diastase and trypsin in the stools.

<sup>30</sup> Loc. cit.

<sup>31</sup> Loc. cit.

4. In the duodenal tube we have the only means of studying a disturbance or inflammation of the duodenum itself.

5. The tube is of value in detecting typhoid carriers.

We wish to express our thanks to Dr. R. W. Knox, of the Southern Pacific Hospital, Houston, on whose service many of these cases were observed, and to Professor M. L. Graves, of the University of Texas, for assistance and encouragement in this work, on whose service the remainder of the cases herein reported were observed.

## SYNCOPÉ.

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Loss of consciousness is directly due to some poorly understood state of the nerve elements of the brain following a change in their relation to their blood supply. It may be thought of possibly as a widespread retraction of cortical dendrites interrupting their connections with all lower centres. It is not due to diminished nutrition of the nerve elements, because while there is enough extravascular plasma in the brain to supply the nerve cells for a not inconsiderable period of time, in the fatal syncope of aortic regurgitation, loss of consciousness and cardiac failure are almost synchronous. More probably it is due to a sudden diminution of blood-pressure within the skull and thus indirectly to a diminution in the blood supply of the brain.<sup>1</sup>

That cerebral anemia will cause unconsciousness has been quite definitely proved experimentally. Kussmaul and Tenner<sup>2</sup> compressed the carotids in a number of male adults and got dilatation of the pupils, slow, deep, and sighing respiration, dizziness and unconsciousness. Leonard Hill<sup>3</sup> produced unilateral convulsions by compression of a single carotid in man; and animals in which he ligated several or all of the cerebral arteries regularly developed convulsions.

The most prominent features of ordinary syncope are due to the action of the heart. The pallor of the face undoubtedly corresponds to anemia of the brain. The patient feels a sense of increasing feebleness, and is often unduly conscious of the action of the heart.

<sup>1</sup> Sir William R. Gowers, A Lecture on Faints and Fainting, *Lancet*, 1907, vol. i, 565.

<sup>2</sup> Nature and Origin of Epileptic Convulsions Which Follow Profuse Hemorrhage, New Sydenham Society, 1859, n.s., 95, p. 28.

<sup>3</sup> Cerebral Anemia, *Philosophic Transactions of the Royal Society*, 1900, B vol. cxciii.

There is often nausea and a sense of prickling of the skin of the face.<sup>4</sup> Sometimes he falls sharply to the ground, though often sufficiently warned by his rapidly increasing weakness to seek the recumbent position. The sight may suffer without loss of consciousness.<sup>5</sup> During the attack the respiration is detected with difficulty and the radial pulse or heart contractions may be imperceptible.<sup>6</sup> The loss and return of consciousness is usually slow, and when regained there is always a correct perception of surroundings.<sup>7</sup>

Syncope frequently occurs in people with normal hearts, and is then indirectly due to various emotions which are induced by impressions usually received through the special senses. Thus certain odors, the sight of blood, an unusual, unexpected, and sudden noise, the touching of some unrecognized and unusual object in a familiar spot in the dark or great fear or sorrow may cause syncope. This emotional fainting is due to inhibition of the nervous system. The constant stream of afferent stimuli to the brain is suddenly neutralized by one all-powerful one with consequent sudden relaxation of muscular tone, collapse of the body, paralysis of the vasomotor system, collection of blood in one set of vessels (the splanchnics), marked diminution in the strength of the contraction of the heart, cerebral anemia, and loss of consciousness.<sup>8</sup> It is not known whether in syncope the heart stops or the contractions become very much weakened<sup>9</sup> or whether its failure is due to diminished blood in its arteries or in its cavities or to diminished blood in the medulla with consequent pneumogastric stoppage.<sup>10</sup> The fact that the sounds are inaudible and the pulse not felt would speak for the latter, though possibly due to extreme feebleness of the contraction.

Mechanical factors play their part in causing a sudden collection of blood in one set of vessels and syncope is not uncommon after withdrawal of peritoneal collections, violent purging, enemata, and paracentesis of the thorax for effusions into the pleural cavity. The release of external pressure apparently causes a sudden paralysis of the walls of the vessels, and if the affected area is large, as is the case with the splanchnics and pulmonaries, enough blood is withdrawn from the general circulation to cause cardiac failure. A similar explanation applies to the syncope of patients who have long been in the recumbent position and are too suddenly raised to the sitting position, but in this case it is the loss of tone of the abdominal muscle that is at fault. Entrance into a warm room from the cold air may cause syncope by sudden withdrawal of blood to the surface of the body.<sup>11</sup> Stooping increases the amount of blood in the head but may sometimes cause momentary unconsciousness.<sup>12</sup>

<sup>4</sup> Gowers, loc. cit.

<sup>6</sup> Allbutt, *System of Medicine*, vol. vi, p. 516.

<sup>8</sup> Leonard Hill, *Further Advances in Physiology*, 1909.

<sup>9</sup> Allbutt, loc. cit.

<sup>11</sup> Lewis, loc. cit.

<sup>5</sup> Ibid.

<sup>7</sup> Gowers, loc. cit.

<sup>10</sup> Gowers, loc. cit.

<sup>12</sup> Gowers, loc. cit.

The vagus is undoubtedly concerned in the causation of certain syncopal attacks. Thus the syncope due to agonizing pain probably occurs through vagus stoppage of the heart rather than through a sudden loss of splanchnic tone, and is more likely to be fatal.<sup>13</sup> Thanhoffer<sup>14</sup> took tracings from students who made pressure on their own vagi. In one case he observed standstill of the heart for over one minute and unconsciousness supervened. Mackenzie<sup>15</sup> reported a case in which there was complete standstill of the heart for four to five seconds, often accompanied by syncope. Neuberger and Edinger<sup>16</sup> reported the case of a patient who had faints while at stool, with a slow pulse. At autopsy there was almost complete atrophy of the right half of the cerebellum and a varicose dilatation of the endymal vessels in the medulla. The rise in blood-pressure while straining at stool probably caused a compression of the medulla near the nucleus of the vagus.

Syncope is frequent in diseases of the heart and vessels. It is well known and may end fatally in fatty degeneration of the heart.<sup>17</sup> In stenocardiac attacks it may take the place of pain. Spasm of the facial muscles with which it is combined allows us to conclude that an active process is going on in the vessels of the cortex as well as in the coronary arteries.<sup>18</sup> In aortic disease it is common. Here the minimal pressure may be quite low, and when the heart is slow and the ventricle weak an extrasystole may cause a dropped beat and abnormal emptying of the arteries.<sup>19</sup> Some of the short attacks of unconsciousness in cerebral arteriosclerosis may be attributed to extrasystoles which are weak in themselves and followed by a slight pause so that the brain is momentarily deprived of blood. This would not occur if the arteries were soft. These short attacks are to be differentiated from ordinary syncope by their abrupt onset and offset and their short duration.<sup>20</sup> Extrasystoles themselves may be the cause of cerebral anemia and syncope. When of the ventricular type they are often so weak as not to overcome the aortic pressure so that the semilunar valves remain closed. A compensatory pause follows, and when such extrasystoles follow every second sinus beat, as not infrequently occurs, the pulse rate becomes only half that of the sinus. With a slow sinus rhythm cerebral anemia and syncope may occur. Paroxysmal tachycardia and paroxysmal fibrillation of the auricles may cause syncope from

<sup>13</sup> Allbutt, loc. cit.

<sup>14</sup> Thanhoffer, Die beiderseitige mechanische Reizung des Nv. vagus beim Menschen, *Centrbl. d. med. Wissen.*, 1875, xiii, 403.

<sup>15</sup> Diseases of the Heart, 1908, p. 345.

<sup>16</sup> Einseitiger fast totaler Mangel des Cerebellums. Varix oblongatæ. Herztod durch Accessoriusreizung, *Berl. klin. Wchnsft.*, 1898, xxxv, 69.

<sup>17</sup> Osler's Modern Medicine, 1907, iv, 220.

<sup>18</sup> Max Herz, Die Herzkrankheiten, p. 191.

<sup>19</sup> Osler's Modern Medicine, 1907, iv, 220.

<sup>20</sup> Herz, loc. cit.

cerebral anemia. The sinus rate itself may be as slow as twenty-five to forty, and such a patient may have syncopal seizures.<sup>21</sup> In congenital cyanosis syncope is not uncommon. Dyspnea is usually a marked feature and frequently culminates in convulsive seizure. A paroxysmal congenital cyanosis has been described by Variot and Sebellean, in which convulsive seizures with dyspnea and extreme cyanosis occur in patients who at other times are quite free from the latter.<sup>22</sup> Syncope and even convulsions are not uncommon in aneurysm of the arch of the aorta, and have been mistaken for epileptic attacks.

Adams-Stokes syndrome is characterized by syncopal or epileptiform attacks, with a slow pulse, and is due in a large percentage of cases to heart block. The attacks may occur in the transition period from incomplete to complete block. At this time impulses entirely cease reaching the ventricle, and a considerable period of time elapses before it starts on a rhythm of its own. In this period no blood reaches the brain, and syncope or epileptiform attacks occur. When block is complete and the idioventricular rhythm established, cerebral anemia may occur from some increased demand on the ventricle. In cases where the conductivity is somewhat diminished, sudden stimulation of the vagus centre may cause the heretofore incomplete block to become complete, with consequent cerebral anemia, until the vagus effect stops or the idioventricular rhythm is established.<sup>23</sup> Syncopal attacks in heart block are marked by pallor, disappearance of the pulse at the wrist, unconsciousness, spasmodic twitching of the muscles of the face, and general convulsions,<sup>24</sup> depending on the length of time during which the ventricle does not contract. In the severest attacks there is squint or conjugate deviation of the eyes, wide pupils, noisy respiration, and frothing at the mouth.<sup>25</sup> The relation between the period of ventricular stoppage and the signs of the resulting cerebral anemia are fairly definite. If it lasts two to two and a half seconds there is little or no disturbance. Thus in simple extrasystole the ventricular pause would not be long enough to cause syncope without the addition of some other factor as cerebral arteriosclerosis or muscular insufficiency of the ventricle. When the ventricle stops for fifteen to twenty seconds, epileptiform convulsions begin and a pause of ninety to one hundred and twenty seconds is rarely followed by recovery.<sup>26</sup>

The stupor and drowsiness seen toward the end in cardiac failure bear only a slight relation to syncope. There is probably some

<sup>21</sup> Lewis, *The Mechanism of the Heart Beat*, p. 265.

<sup>22</sup> Osler's *Modern Medicine*, 1907, iv, 325.

<sup>23</sup> Hirschfelder, *loc. cit.*, p. 561.

<sup>24</sup> Osler's *Modern Medicine*, 1907, iv, 220.

<sup>25</sup> *Ibid.*

<sup>26</sup> Thomas Lewis, *loc. cit.*, p. 266.

cerebral anemia from failure of the left ventricle to properly fill the arterial system, but there is also a chronic poisoning with carbon dioxide.<sup>27</sup>

True syncope is to be differentiated from minor epilepsy, which it may much resemble. Indeed, strong evidence has been offered to show that repeated cardiac syncope has a disposing influence to epilepsy. This suggests that the state of the nerve elements concerned in loss of consciousness may from frequent inductions show a tendency to spontaneous development.<sup>28</sup>

In cardiac syncope the loss and return of consciousness is more gradual than in epilepsy, and the beginning of the attack is marked by pallor, which never occurs in petit mal. Pallor may follow loss of consciousness in epilepsy, but usually there is no change in the color of the face. There is no disorientation on return of consciousness after syncope, the patient immediately recognizing his surroundings. Differentiation is sometimes made difficult by the fact that although external influences are usually the cause of syncope, epileptic attacks may also be brought on by them. In epilepsy the aura may be cardiac. Even sudden change of position and stooping have been known to bring on epileptic attacks as well as cardiac syncope.<sup>29</sup>

<sup>27</sup> Osler's *Modern Medicine*, 1907, iv, 220.

<sup>28</sup> Gowers, *loc. cit.*

<sup>29</sup> *Ibid.*



## REVIEWS

DIE THIERISCHEN PARASITEN DES MENSCHEN. By DR. MAX BRAUN, O. O. Professor der Zoölogie und vergl. Anatomie, Direktor des Zoölogisch. Museums der Universität Königsberg I.Pr., Geh. Regierungsrat, und DR. OTTO SEIFERT, A. O. Professor f. Rhino-Laryngologie, Vorstand der Poliklinik f. Nasen- und Kehlkopfkrankhe der Universität Würzburg. Part I, Naturgeschichte der Thierischen Parasiten des Menschen. DR. MAX BRAUN. Pp. 559; 407 illustrations. Würzburg: Von Curt Kabitzsch, 1915.

THE present work is to be of a monumental character, and like all works originating from the present source, every detail is carefully and completely worked out, and therefore it is a pleasure and benefit to read and study. The volume is so profusely illustrated that almost every other page contains one or more drawings, diagrams, or photographs to illuminate the excellent text. The subject is introduced by a general discussion of parasites and parasitism. The author views the subject "the animal parasites of man" under the following main headings: Protozoa; plathelminthes; nematodes; acanthocephali; gordiacei; hirudinei; arthropoda. Protozoa are divided into a large number of headings, which are reviewed under the general classification of rhizopoda, and includes the various entameba, ameba, and paramoeba; flagellata; onidosporidia; sporozoa; and infusoria. Plathelminthes are divided into the main headings of trematodes and cestodes. The arthropoda group is divided into two main parts, arachnoidea and insecta. All of the various animal parasites are described, including not only those that attack the various internal organs and structures, but also those that crawl on the surface of the skin and others that migrate in the integument. There is a striking difference in the size of the various animal parasites if one considers those which are microscopic; for instance, the gastrophilus larva, which is pin-point in size, and the guinea worm (*dracunculus*), which may be over thirty inches in length. One of the most valuable features of the volume is the complete bibliography; ninety-five pages are devoted to all of the literature extant on the subject of animal parasites. It gives the reviewer pleasure to recommend this admirable book to anyone interested in this rapidly-growing and until recently, comparatively little-touched field of medicine. F. C. K.

THE PRACTITIONER'S VISITING LIST FOR 1916. Four styles, weekly, monthly perpetual, sixty-patient. Philadelphia and New York: Lea & Febiger.

WE again welcome the appearance of this useful volume. Like its predecessors, the *Practitioner's Visiting List for 1916* contains much practical information of the sort that physicians constantly need, arranged in a way to make it quickly and easily accessible. Such data as the ligation of arteries, tables of dosage, methods of examining urine, and comparative scales showing the equivalent in the metric system of ordinary weights are measures to be mentioned among the topics touched on. The essential feature of this book is the visiting list, which is admirably adapted to the most exacting needs of the busiest practitioner. G. M. P.

CASE HISTORIES IN DISEASES OF WOMEN, INCLUDING ABNORMALITIES OF PREGNANCY, LABOR, AND THE PUERPERIUM. By CHARLES M. GREEN, A.B., M.D., Professor of Obstetrics and Gynecology in Harvard University; Senior Surgeon for Diseases of Women, Boston City Hospital. Pp. 477; 11 plates, 1 cut, and 25 charts. Boston: W. M. Leonard, 1915.

THE author, a pioneer in the case history method of teaching, presents a systematic review of the pathological processes of the female reproductive organs from infancy to senility. The subject matter is divided into five parts. In each section we find a brief yet comprehensive consideration of the predominant morbid processes peculiar to the period of a woman's life under discussion. These are grouped in each section as Functional Disorders, Malformations and Displacements, Infections, Traumata, and Neoplasms. Following the sectional introduction are the illustrative case histories and appended to each is a short comment on the various features of the case.

Section one reviews the conditions encountered during infancy and childhood. Eight histories serve to make clear the various disorders. The histories are abstracted to include the history of the diseased condition, the diagnosis and prognosis, method of treatment, and the comments.

Section two takes up puberty and adolescence. The disorders of menstruation are considered fully, and among the twenty-two illustrative case histories are typical examples of the various forms of amenorrhea and dysmenorrhea.

Section three deals with the morbid conditions of maturity.

This section comprises over two-thirds of the text and includes the histories of one hundred and thirty-three cases.

References to abnormalities of the reproductive processes are very complete. The author evidently treats the toxemia of pregnancy in a very conservative manner, and is opposed to any local measures in puerperal sepsis. Febrile conditions in the puerperium, aside from sepsis, scarcely mentioned in some text-books, are illustrated by histories and temperature charts. The graphic description of pelvic infections is an interesting part of the introduction to the section. Malignant disease of the pelvic organs receives full attention.

Section four reviews the decline of the sexual life of woman, the climacteric, and the eleven histories detail the most frequently encountered pathology.

Section five, on anility, completing the volume, brings up the occasional atrophic lesion in those whom the author considers "old women."

The book is an interesting one, the histories are instructive, many excellent suggestions in treatment are given, and there is often a pleasantly personal tone to the comments.

The volume will rank high in the Case History Series, and will be of interest and service to anyone whose practice includes the care of women.

P. F. W.

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EXERCISE IN EDUCATION AND MEDICINE. By R. TAIT MCKENZIE, A.B., M.D., Professor of Physical Education, and Director of the Department, University of Pennsylvania. Second edition; pp. 585; 478 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THIS new edition of Dr. McKenzie's well-known work is sure to have an even greater success than at its earlier appearance. More and more attention is yearly being paid to exercise, not only to its value in general, but to the importance of careful and scientific control of its quality and quantity. Exercise can no longer be advised in a vague, indefinite manner: it must be adapted to the individual and fitted to special needs. A faulty prescription for exercise may be as harmful as any therapeutic error, while exercise properly employed may cure certain ills when all other measures fail. The normal child and adult, the scoliotic, the tabetic, and the cardiac can all exercise with benefit, but not in the same manner or amount. If this book contained no more than this information it would appeal to few outside the medical profession. However, it contains much more, and includes in the first part (320 pages) a thorough discussion of the various systems of physical

training employed abroad and detailed descriptions of methods of physical education in schools, colleges, municipal playgrounds, etc. Special chapters are devoted to the physical education of the blind, the deaf-mute, and of mental and moral defectives. Part II covers the subject of exercise in medicine, and describes, almost too conservatively, what can be accomplished by exercise in the treatment of flat-foot, club-foot, visceroptosis, constipation, respiratory diseases, diseases of the circulation, obesity, tic, stammering, chorea, and other conditions. There is no need in going further. The work is all inclusive, well written, and lavishly illustrated. Except for an amusing misprint in a quotation from Solon on the front page, the printer has done his work well. The author, Dr. McKenzie, is at present in England at one of the large training camps, so we may look forward to additional chapters on military training in future editions.

O. H. P. P.

MEDICAL ELECTRICITY, ROENTGEN-RAYS, AND RADIUM, WITH A PRACTICAL CHAPTER ON PHOTOTHERAPY. By SINCLAIR TOUSEY. A.M., M.D., Consulting Surgeon to St. Bartholomew's Clinic, New York City. Second edition, thoroughly revised and enlarged, Pp. 1219 798 illustrations, 16 in colors. Philadelphia and London: W. B. Saunders Company, 1915.

THE author is recognized as an authority by those engaged in the practice of electrotherapeutics and roentgenology. Possibly only those who are familiar with these subjects can appreciate the stupendous undertaking represented in the compilation of a book of this kind. Although this is a new edition which is supposed to be thoroughly revised, it must be truthfully stated that the book is not up-to-date in several respects. The subject of roentgenology alone is broadening so rapidly, and ideas and methods are changing so constantly and extensively, that it is almost beyond the power of any one individual to keep a book as comprehensive as this one is supposed to be thoroughly abreast of the times. The roentgenologist can realize this and can make allowances, but the student or beginner may be easily mislead into false impressions. Gastro-intestinal diagnosis is one of the most important branches of roentgenology at the present time, but the author deals with it in a very unsatisfactory and incomplete manner. He states that he is strongly opposed to the use of the fluoroscope in gastro-intestinal diagnosis, whereas this method is now generally recognized as being absolutely essential for the diagnosis of many conditions of the digestive tract. There is much valuable data concerning roentgen diagnosis and treatment that might well be substituted for much information the book contains that is of comparatively little value.

More than half the space is devoted to the physics and physiological effects of electricity and to electrotherapeutics. A short section deals with phototherapy and another with radium and its applications. A large part covers the subject of roentgen diagnosis and therapy.

H. K. P.

**A MANUAL OF SURGERY.** By FRANCIS T. STEWART, M.D., Professor of Clinical Surgery, Jefferson Medical College; Surgeon to the Germantown Hospital; Out-patient Surgeon to the Pennsylvania Hospital, Fourth edition. Pp. 774; 580 illustrations. Philadelphia: P. Blakiston's Son & Company, 1915.

THE fact that this work has gone to its fourth edition does more to show its true worth and popularity than any criticism the reviewer may make. This last edition more fully elaborates on the more recent advances in surgery. Bronchoscopy, esophagoscopy, proctoscopy, roentgenography all have been expanded. Transfusion, hemorrhage, spinal puncture, colectomy, hernia, tumors of the hypophysis, and surgery of the lung, liver, stomach, spleen, and breast all have been revised and brought to date as regards their diagnosis and treatment.

New sections on the exclusion of the pylorus, sporotrichosis, surgical purpura, and hand conditions, and transplantation of fat, fascia, bone, and veins have been added.

Many new illustrations have been added and some old ones discarded. One really adverse criticism is that even now the author wastes valuable space with many illustrations that are not appropriate for students and practitioners. The book, however, is an excellent one, and with the exception of a few ideas on fracture treatment, will serve admirably for general use.

E. L. E.

**DIABETES MELLITUS.** By NELLIS B. FOSTER, M.D. Pp. 243. Philadelphia: J. B. Lippincott Company, 1915.

IN the first chapter of this volume the author presents in a clear and concise way the principal factors that govern the general metabolism of the animal body. The subsequent three chapters are devoted to a discussion of the role of glucose in the animal body, experimental glucosuria, and the influence of glucose on the metabolism of fats and acidosis. The author then proceeds with a discussion of the pathogenesis, history, etiology, and pathology of human diabetes. The last one hundred pages are devoted to a description of the symptoms, diagnosis, and treatment of the

disease, with a final chapter on the chemical methods of identifying and determining sugar in the urine and blood.

This work is recommended to the practitioner of medicine for two reasons: First, because it will enable him to better understand and manage a disease which he is frequently called upon to treat, and secondly, because it will give him an insight into the perplexities of the problems which so baffle the medical investigator.

A. I. R.

WHEELER'S HAND-BOOK OF MEDICINE. By WILLIAM R. JACK, B.Sc., M.D., F.R.E.P.S.P., Assistant Physician to the Western Infirmary of Glasgow. Fourth edition; Pp. 538. New York: William Wood & Co.

THE fourth edition of this small volume on the whole of the great subject of internal medicine, sets forth the salient features of disease in a careful and thorough manner. The book has been carefully revised since the last edition four years ago and has been brought up to date for the most part very satisfactorily. There are but few omissions of what is essential and but few mistakes or errors in the subject matter. The various diseases are dealt with in a most systematic though extremely dogmatic and didactic manner, as would be expected in a book of this type, so that it presents the subject of medicine in such a form as would be of practical value to a medical student. To a general practitioner, however, the value of such a book is extremely doubtful, certainly it would be of no real worth to a man, keen enough to desire to know more than the barest and briefest facts about some unusual or interesting case.

J. H. M., JR.

PRINCIPLES OF HYGIENE: FOR STUDENTS, PHYSICIANS, AND HEALTH OFFICERS. By D. H. BERGEY, M.D., First Assistant, Laboratory of Hygiene and Assistant Professor of Bacteriology, University of Pennsylvania. Fifth edition; pp. 531; illustrated. Philadelphia and London: W. B. Saunders Company, 1915.

THIS new edition remains in aim and plan of arrangement the same excellent volume that its predecessor was, although many of the chapters have not been changed, still others dealing with subjects undergoing marked changes at the present time, have been revised and brought up to date.

This is especially true of that portion of the book dealing with the removal and disposal of sewage. Much of this chapter has been omitted, while a new diagram and some discussion of the

Emscher tank has been inserted. A new short chapter on nutritional diseases treats in brief fashion of beriberi, pellagra and scurvy. Antityphoid vaccination with an interesting reference to the results obtained in our own United States Army is a feature in this edition. A chapter on the transmission of relapsing fever and one covering interstate quarantine laws are additions worthy of note.

In the table of contents the divisions of body and foot inspection should exchange positions, and the page references should be corrected. These headings appear under the main chapter dealing with military hygiene, one which we are sure will be most thoroughly revised after the present struggle abroad. We hope the future sixth edition will continue to maintain the excellent standard of the present one. The book undoubtedly presents, as its author intends it to do, the practises of modern hygiene in a short, lucid, tangible style. The students in architecture, public health, sanitation, and medicine should find it a valuable aid in their work.

T. G. S.

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DETECTION OF POISONS AND POWERFUL DRUGS. By DR. WILHELM AUTENREITH, Professor in the University of Freiburg. Translated by WILLIAM H. WARREN, Ph.D., Professor of Chemistry in Wheaton College. Fourth edition; pp. 320; 25 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

TEN years have elapsed since the previous edition of this work was printed. The changes manifested in the present edition indicate the tremendous advance made in "Detection of Poisons." This new edition is larger than the last one by 100 pages.

The seven chapters now comprising the book have undoubtedly been painstakingly revised. The first three chapters remain unchanged only in arrangement. Such drugs as hydrastin, veronal, cantharidin, cytisin, ergot, papaverin, pilocarpin, saponin substances, salamin, thebarin, and the toxalbumins ricin, abrin, and croton, are all discussed for the first time in these chapters.

The changes in the subsequent chapters have added very positively to the value of the book not only as a laboratory manual for students, but as a guide for those wishing to make practical use of the procedures described. Most that is new in the book appears in the fifth chapter, which treats of special methods in analysis.

The present edition is a faithful translation on the whole of the original German text. The translator has added, on a few occasions, some personal opinions to the subject matter of the parent treatise, *e. g.*, the introduction of the Gutseit method of estimating the quantity of arsenic and antimony. This present German edition has been translated into English, Spanish, and Italian—a

most complimentary tribute to any book, indicating the favorable manner in which it has generally been received. Both the author and translator have done their work well and have made a valuable contribution to medicine.

T. G. S.

DIRECT LARYNGOSCOPY, BRONCHOSCOPY, AND ESOPHAGOSCOPY. By DR. W. BRÜNING. Translated and Edited by W. G. HOWARTH, Surgeon-in-Charge of the Throat Department at St. Thomas's Hospital. Pp. 367; 114 Illustrations. New York: William Wood & Co.

THIS book is a revised and expanded edition of Brüning's *Handbuch f. die Technik und Methodik der directen Okularen Methoden*, and furnishes to the student in this comparatively new and rapidly expanding field of clinical work an excellent description of the necessary instruments and technique and the indications for their use. The first chapter, consisting of fifty-six pages, is devoted to the instruments which the author considers essential and their management. The indications for and the best methods of inducing anesthesia, local and general, are discussed, as well as the uses, advantages, and methods of giving oxygen inhalations. The remaining and greater portion of the book is devoted to the consideration of direct laryngoscopy, tracheobronchoscopy, and esophagoscopy, with sixty-seven pages on bronchoscopic operations and methods of treatment. The advances made in methods of direct inspection of these concealed portions of the body, particularly of the trachea and bronchi, are so important that not only the specialist but the general surgeon and physician will find it necessary to know more about them. It is interesting and important to know with what effectiveness local anesthesia can be employed in this method of investigation, that painting with a cocaine solution is more effective than spraying, and that a patient "had frequently been given as much as fifteen brushes of 20 per cent. cocaine solution," which is fifty times the so-called maximum dose. Direct exposure is rendering possible cures which were previously impossible. The passage of a bougie through a small eccentric opening in an esophageal stricture and the removal of a foreign body from a bronchus may now be done with precision and safety. The author is one of the acknowledged masters in this field, while the translator and editor has given us a lucid and readable translation which will be appreciated particularly by those who are fitting themselves for work in this special field.

T. T. T.



# PROGRESS OF MEDICAL SCIENCE

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## MEDICINE

UNDER THE CHARGE OF

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**Studies on the Mechanism of the Secretion of Urine.**—E. LESCHKE (*Ztschr. f. klin. Med.*, 1914, lxxxi, 14) reports important experiments which he had made on the secretory activity of the kidneys, by means of histo-chemical tests which the author has devised. He is able to determine which cells secrete certain normal constituents of urine by methods which fix the solids in the cells. Thus, he has studied the secretion of chlorides, phosphates, urea and urates. He has also studied the secretion of iodide. His methods appear to be specific. It is only the cells which excrete these salts which show the reaction. By giving the experimental animals large quantities of water, the urine is so diluted that the specific reaction practically disappears, to become more intense, the more concentrated the urine is. The reactions are not found in other tissues except the stomach where the marginal cells show the chloride reaction; the chief cells lack it. The author summarizes his results and those reported in literature as follows: (1) Previous experiments to determine the mechanism of the excretion of dyes have shown that the greater part is excreted by the uriniferous tubules. To what extent the glomeruli are concerned remains unsettled. (2) The author's experiments, as well as those of other workers, have shown conclusively that salts foreign to the body (ferrocyanids and iodids) are excreted solely by the renal tubules, while the glomeruli themselves do not show evidence histo-chemically of excretion even when an excess of work is thrown upon the kidneys by injection of large amounts of salt. (3) By means of the author's histo-mechanical methods it is possible to demonstrate the point where the principle constituents of normal urine are excreted. (4) The excretion of chlorides, phosphates, urea, uric acid and purins takes place chiefly only in the specific excret-

ing cells of the convoluted tubules, and of the transitional portion connecting them with the descending straight tubules. Fahr's secretion granules, which disappear during hunger, are found in the same cells. (5) The glomeruli excrete water in physiological solution. The small quantities of salt and of other urinary solids corresponding to a physiological solution are also excreted by the glomeruli. (6) When the kidneys are forced to do increased work through injection of salt, urea, or purins, the excretion of the same is still exclusively by the same specific cells. The glomeruli, under these conditions, still excrete only water in physiological solution. (7) The ability to concentrate or dilute the urine rests entirely with the specific excreting cells or tubules. (8) Bowman's theory of the secretion of urine is fully confirmed. To what extent water is reabsorbed from the kidney's as Ludwig supposed, is undetermined.

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**On the Excretion of Creatin and Creatinin in Diabetics and Nephritics.**—D. LAMPERT (*Ztschr. f. klin. Med.*, 1914, lxxx, 498) has made a study of the excretion of creatin and creatinin in diabetics and nephritics. He employed the Autenrieth and Müller method and all patients were on a meat-free and bouillon-free diet during the periods of observation. In healthy adults, he found the daily average excretion of creatinin to be between 0.9 and 2.4 gm., the majority being between 1.2 and 1.5 gm. Creatin was usually entirely absent, and, when present only in traces (0.02 mg.). In diabetics, the values for creatinin were usually lowered or at the lower limit of the normal. With few exceptions creatinin was found to an amount less than 1 gm. though in several cases 1 to 1.2 gm. was found. In diabetes gravis with a high grade of acetonuria, creatin was practically always found in the urine, usually more than 0.2 gm. (on two occasions 1 and 1.2 gm.). In diabetes levis with traces of acetone, creatin in two cases was lacking or present only in small amount (less than 0.3 gm.). In nephritics (five cases), the author found a decrease in creatinin constantly, even when there was a diuresis and only slight impairment of function. Creatin was found in only one case, in which there was marked renal insufficiency, and then only in small quantity (maximum 0.15 gm.). Two cases of diabetes complicated by chronic interstitial nephritis were characterized by an especially low creatinin value. Low creatinin values were also observed in a case of cancer of the liver with cholemia; creatin was also present in small amount (0.1 gm. or less). The author thinks it is plausible to attribute the large quantities of creatin found in the urine of diabetics with acidosis to a disturbance of metabolism and the diminished output of creatinin in nephritics to renal insufficiency. The generally accepted view that acidosis is the result of deficient oxidation of the acetone bodies suggests the idea that the increase in creatin is also due to a disturbance of intermediary metabolism. The findings in the nephritics suggest the use of this method in functional renal diagnosis.

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**On the Significance of Cholesterin in the Origin of Giant-cell Tumors of the Tendons and Joints.** S. WEIL (*Berl. klin. Wchnschr.*, 1915, lii, 129) refers to the recent work of several authors which have demonstrated an increase of cholesterin in the blood in patients having

xanthomas, even the simple lid xanthomas. In all of these lesions, the so-called xanthoma cells are found. Their dotted or foamy appearance is due to deposition of cholesterol. The author has been interested in the histological study of xanthosarcomata of tendons and joints. In a recent typical case, he had the blood examined for cholesterol, and it was found that it contained 0.27 mg. per c.c. (normal 0.14 to 0.16 mg. per c.c.). He suggests the need of further examination to determine whether this metabolic anomaly is constantly associated with the presence of xanthosarcomata.

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**The Therapeutic Use of Aqueous Extracts of Leukocytes in Lobar Pneumonia.**—WILLIAMS and YOUNG (*Jour. Med. Research*, 1915, xxxi, 391) report the results of the treatment of seven cases of lobar pneumonia with aqueous extracts of leukocytes, as suggested by Hiss. In contradistinction to the reports of numerous other observers, the authors were unable to observe any definite evidence in their cases that such extracts exert a modifying influence upon the temperature and a lessening of the symptoms which are usually considered of toxic origin. Of the seven patients, four died, and of these, two were alcoholic. They were unable to detect any differences in the results, whether the patients were given repeated uniform doses, steadily increasing doses, single moderate doses or single large doses, but in all patients, with one exception, the total amount of the extract used was large. No effects were observed upon the temperature, pulse or leukocyte count, regardless of how early in the disease the treatment was begun. The duration of the disease and the manner of its termination were about the same as one would observe in a similar series of untreated typical cases of lobar pneumonia.

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**Varieties of Pneumococcus and Their Relation to Lobar Pneumonia.**—As the result of their studies, DOCHEZ and AVERY (*Jour. Exper. Med.*, 1915, xxi, 114) have shown that the pneumococci which can be isolated from individuals suffering from lobar pneumonia fall into four definite pathological groups which they have arbitrarily numbered from 1 to 4. The members of the first three groups appear to be related closely to each other, so far as one can judge from certain immunological reactions, while the members of the fourth group consist of independent varieties not definitely related to one another by the immune reactions employed. Thus far the authors have observed no change from one type into another nor any tendency of these organisms to lose their specific character. The groups vary distinctly in their pathogenicity for human beings, the order of their virulence being as follows: Groups 3, 2, 1, 4. On the other hand the degree of protective power which is developed in the sera of animals immunized against the various groups varies inversely with the virulence and the amount of capsular development. A careful study of the sputum from a series of normal individuals failed to reveal in any case an organism which could be grouped with any of the fixed types of pneumococcus. All of those found exhibited the same characters as those organisms which belonged to Group 4. These are of low virulence and cause only about 20 per cent. of the cases of pneumonia, hence it may be safely assumed that the majority of cases, particularly the more virulent ones, are due to organisms not

found in normal mouths. The only exceptions to this observation have been limited to a group of healthy individuals who have been intimately in contact with cases of lobar pneumonia. From such individuals organisms belonging to the typical groups have been isolated in a number of cases. Such individuals may safely be regarded as healthy carriers of disease-producing types. Dochez and Avery conclude from their study that probably the majority of the cases of pneumonia are dependent upon their direct or indirect contact with a previous case, that mere infection of the mouth by virulent types is not sufficient to cause the disease but that circumstances favorable to their invasion of the lungs must arise during the period when they are harbored in the mouth. From certain comparative studies they make the suggestion that strictly parasitic races of microorganisms are pure lines and have established themselves as parasites during a period of high racial susceptibility.

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**The Effect of Pituitary Extract upon the Secretion of the Cerebrospinal Fluid.**—WEED and CUSHING (*Amer. Jour. Physiol.*, 1915, xxxvi, 77) have attempted to answer the question as to whether drugs which appear to increase the flow of the cerebrospinal fluid act directly on the choroid plexuses, or is their influence exerted on the cerebral capillaries in such a way that an increased amount of fluid is poured out through the perivascular lymphatics. In this study the authors have hit upon a far simpler method than those which have been previously employed. This consists of introducing a calibrated needle into the third ventricle by a callosal puncture. The experiments which are reported, were conducted either upon dogs or cats and all the injections were made intravenously. The results may be summarized as follows: when extracts of the posterior lobe of the hypophysis are introduced intravenously, they serve to discharge cerebrospinal fluid from the calibrated catheter introduced in its pathway. Positive results occur following the injection of nearly all the fluid proprietary preparations, but the desiccated extracts have tended to be more active. This increased secretion occurs under variable conditions and seems to be independent of respiratory or blood-pressure influences, for it has been observed to coincide with periods of respiratory cessation and in conditions of both hyper- and hypotension. An increased flow may even continue after the death of the animal. The evidence leads the authors to believe that the increased outflow under these experimental conditions represents the actual secretory response rather than an expulsion of preformed fluid, and they conclude that extracts of the posterior lobe of the hypophysis produce choroidorrhea by stimulating the secretory activity of the choroid plexus.

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**The Clinical Aspects of Syphilis of the Nervous System.**—In a rather extensive article HEAD and FEARNSIDES (*Brain* 1914, xxxvii, 1) go over the very important subject of central nervous system syphilis, illustrating the various points which they wish to bring out, by suitable case records. The importance of a careful history of the primary infection, the early symptoms and signs of cerebrospinal syphilis, the serological findings in the various stages, and other valuable points are well brought out. These may be summarized as follows: All the manifestations of central nervous system syphilis are consequent on the direct

activity of *Spirocheta pallida*, and the clinical picture depends upon the situation of this activity and the susceptibility of the tissues. When the infection is mainly within the essential structures of the central nervous system, both neuroglia and nerve elements participate in the tissue reaction which results in the death and degeneration of certain systems of cells and fibers to which may be ascribed the greater part of the clinical manifestation. The authors believe that the more closely the clinical signs and symptoms point to pathological changes in the meninges and vessels, the more certainly will the disease yield to suitable treatment, while the reverse is true when the clinical symptoms point to one or more parenchymatous foci. The Wassermann reaction in the spinal fluid in the meningovascular form depends upon whether the spinal or basal meninges are involved, and the reaction tends to be negative or weakly positive when the disease is limited to the intracranial contents. In cases of syphilis centralis a strong Wassermann reaction is usually observed, as long as the disease is active. The former type of cases can usually be made Wassermann negative within six months under treatment with salvarsan or neo-salvarsan, while the latter type is not apt to yield to any of the present forms of anti-syphilitic treatment. They are of the opinion that no complete diagnosis or prognosis can be made until the patient has been under observation and treatment for at least six months, during which time the cerebrospinal fluid has been systematically examined. No matter what the situation and nature of the lesion is, some secondary degeneration will almost certainly result and therefore some of the signs and symptoms are not apt to be altered by any treatment, hence the importance of making the diagnosis of syphilis early, so that therapy may be employed before the advent of the secondary stages.

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**Survival and Virulence of the Microorganism Cultivated from Polyomyelitic Tissues.**—FLEXNER, NOGUCHI and AMOS (*Jour. Exper. Med.*, 1915, xxi, 91) describe in the present paper a strain of the organism isolated from a case of polyomyelitis thirteen months ago. They are able to show the following interesting points: The organism has both survived and maintained its pathogenicity in cultures for over a year. Though the primary inoculation of this strain into monkeys may fail to produce polyomyelitis, the disease follows from the effects of successive injections and the lesions occurring in the spinal cord, medulla and ganglia are precisely the same as those which are found in the nervous system of animals which react to the injection of ordinary virus. The glycerinated nervous tissues derived from these monkeys which only develop the disease after several injections, are capable of transmitting the disease to monkeys upon intracerebral inoculation and from these animals the microorganism may be recultivated. The organism may be made to grow with difficulty under saprophytic conditions. Once this change has been affected, its growth occurs readily upon suitable media. If such an organism is reinoculated in the monkeys, the parasitic peculiarities of the microorganism are restored, for it then displays the marked fastidiousness to the artificial conditions of multiplication present at the original isolation. These experiments afford strong additional evidence in support of the view that this organism bears a close etiological relationship to the human and experimental polyomyelitis.

**Isolation and Cultivation of the Tubercle Bacillus from the Sputum and Feces.**—Dissatisfied with the lack of uniformly positive results when using the methods commonly employed, PETROFF (*Jour. Exper. Med.*, 1915, xxi, 38) has devised a new and simple method by which the isolation of the tubercle bacillus is rendered easy and certain. Thus 69 positive cultures were obtained from the sputum of 69 patients in all stages of tuberculosis. Of the specimens 6 were negative by direct microscopic examination; 49 positive cultures were isolated from 32 specimens of feces. From a series of experiments it was determined that a special medium containing gentian violet is the most satisfactory one to use. The details for the preparation of this medium are given in full. Moreover it is pointed out that under the most favorable conditions it takes at least six days for a single tubercle bacillus to grow to a visible colony. The method as applied to the isolation of the bacilli from the sputum consists in mixing equal parts of sputum and 3 per cent. sodium hydroxide. After being well shaken the mixture is placed in an incubator for a half-hour. It is then neutralized with normal sterile hydrochloric acid, centrifugalized, and the sediment inoculated in the media described. Most of the specimens gave positive results in seven days, though some took twelve to fourteen, but never longer. The colonies may appear violet, while others are capable of decolorizing the medium. A method for the isolation of the bacilli from the feces is described. It should be noted that the growth from the feces appears much more slowly than from the sputum, colonies appearing on the average of from two to three weeks after the inoculations are made.

## SURGERY

UNDER THE CHARGE OF

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**The Reformation of Gall-stones after Operation.**—STANTON (*Ann. Surg.*, 1915, lxi, 226) says that notwithstanding the relative frequency of clinical recurrences following gall-stone operations, actual reformation of stones in the gall-bladder or ducts following their removal by operative methods is of extremely rare occurrence. He reports a case of definite reformation of stones in the gall-bladder after cholecystotomy and a general summary of the available data concerning this phase of gall-stone surgery. If no foreign body is left in the gall-bladder or ducts after the operation, the reformation of gall-stones is so rarely

observed as to constitute almost a negligible factor in gall-bladder surgery. The reported cases do not bear out the assumption that cholecystectomy affords a much greater immunity against reformation of calculi than does cholecystotomy. Adequate care should be exercised not to leave threads from gauze sponges nor unabsorbable suture material in the gall-bladder or ducts at the close of the operation. The data consulted during the preparation of this paper has further strengthened Stanton in the belief that the two most important factors in determining the end-results of gall-bladder surgery are the complete removal of the calculi and the maintaining of sufficiently prolonged postoperative drainage. In the absence of organic duct strictures he believes that the question of cholecystotomy *vs.* cholecystectomy is largely one of technical expediency in individual cases. In many badly diseased gall-bladders it is easier and safer to remove the gall-bladder than to try to remove all of the stones and fragments of stones from the gall-bladder *in situ*, and the same is often true of gall-bladders containing great numbers of minute stones and cholesterin particles.

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**Acute Hemorrhagic Pancreatitis.**—DYAS (*Surg., Gynec. and Obst.*, 1915, xx, 211) says that a positive diagnosis of acute hemorrhagic pancreatitis cannot be made with absolute certainty, since we still lack a distinct pathognomonic sign for this disease. Laboratory aids, such as the Cammidge reaction and the Wohlgemuth diastase blood-test are of no value in this condition. A tentative or probable diagnosis can be made in a certain number of cases, provided a careful history is obtainable and the various phenomena, as they present themselves are properly interpreted. The most striking feature of this condition, clinically, is the evidence of peritoneal disturbance in the upper abdomen, the so-called "acute abdomen" which all surgeons agree is an indication for surgical interference; and acute hemorrhagic pancreatitis should always be borne in mind in such cases. When finding the peculiar odorless, serosanguineous fluid and the small flecks of fat necrosis, it is direct and undoubted evidence of acute hemorrhagic pancreatitis. The best results are obtained in cases in which operation precedes the stage of necrosis or pus formation. Hence, early surgical interference in all such cases will be rewarded by more frequent recoveries. The writer's personal observation of the intense cyanosis of the distended small intestines, with the peculiar granular or gritty feel of the thickened great omentum, has helped him in many cases to recognize the condition at operation, and look to the pancreas at once as the cause of the trouble. This is of special value in cases operated upon for supposed intestinal obstruction. The abdomen opened, the condition should be looked for and recognized quickly. Then prompt and sufficient drainage should be instituted, causing the patient as little shock as is compatible with good surgical technique. The high median incision is the best one to use, because it is the most favorable for exploratory purposes. The lumbar incision has its indications, but is only rarely resorted to, and then usually in late cases when abscess is pointing in the lumbar region. Postoperative hemorrhage is not an infrequent cause of death. It is due to necrosis, usually occurring in late cases. Therefore, early operation and gentle manipulation is the prophylactic treatment for this unfortunate complication.

**Report of the Committee of the American Surgical Association on the End-results of Fractures.**—ESTES (*Ann. Surg.*, 1915, lxii, 278) as chairman reports for the committee the following recommendations: As a general principle fractures should be treated by a skilled surgeon. Roentgen-ray should be employed by a competent radiographer, or a fluoroscope should be used for diagnostic purposes before the permanent dressing is applied. At least two roentgenograms should be taken, and they should be taken from opposite perpendicular directions. Roentgenographs should be taken also after permanent dressings are applied to prove proper reduction, and at the end of the treatment to show the result of the union and for the purpose of a graphic record. Fractures should be reduced immediately after the injury if possible, to obtain and apply proper retaining apparatus or splints. The statistics show markedly better results when the treatment is begun at once. It is, however, not only useless but cruel to subject the patient to the pain of manipulation for reduction unless the surgeon has proper fixation apparatus at hand and the patient is where he may have a permanent dressing applied. General anesthesia should be employed as a rule to facilitate reduction and prevent pain, unless the condition of the patient contra-indicates it. Neither the operative nor the non-operative treatment is to be recommended exclusively. Each has its indication and should be employed when required. Generally speaking, the age period under fifteen years is the period in which non-operative methods are especially effectual. In the other age periods up to sixty years, operative methods may with confidence be employed when non-operative treatment has proved ineffectual in reducing, or controlling the fragments in proper position. The operations should not be delayed longer than one week after the injury. It may be used at any period, except in senile cases, whenever a roentgenogram shows a deformity or a position of the fragments which obviously cannot be reduced or when proper efforts at reduction and retention have proved unavailing. Some form of rigid plate applied directly to the bone or an Albee "inlay" seems to be the best fixation method in operative cases. Open operations for simple fractures should be undertaken only by experienced surgeons who are thoroughly equipped by training and who have proper instruments and apparatus to meet all the possibly indications of the operation.

**Autoplastic Repair of Fractures of the Neck of the Femur.**—DAVISON (*Ann. Surg.*, 1915, lxii, 284) reports two cases of fracture of the neck of the femur. In one patient, fifty-six years of age, a bone transplant was employed, and in another, fifty-four years of age, a large metal screw was used to fix the fragments. The first died twenty-three days after operation and the second, twenty-five days afterward. The pathological specimen from the first showed good union at the line of fracture, while that from the second showed only fibrous union. Davison concludes that: Autoplastic transplantation of bone is the best treatment for both recent and ununited fractures of the neck of the femur, unless contra-indicated by age or condition. The fibula furnishes the transplant of choice. The transplant impinging on the points of compact bone described will graft to these points of leverage



and give strong support to line of fracture. The transplant imbedded in cancellous bone will stimulate the production of osteoblasts and the growth of new semicompact bone in the cancellous area around the transplant, grafting them together by bony union. The transplant must be completely immobilized until it has grafted to the recipient bone. The position of immobilization must be extreme abduction and external rotation of the thigh. The plaster cast to be effective must extend from the axilla to the toes on the injured side and also include the opposite thigh in abduction.

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**The Treatment of Hip-joint Tuberculosis and its Results.**—STOLLER (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 54) studied the cases treated in Kocher's clinic in Bern and in his private clinic, between 1890 and 1913. Manninger collected and studied the cases treated between 1887 and 1900, but some of the cases between 1890 and 1900 were not at his disposal. Only such cases during this ten-year period are to be found in Stoller's group which include 63 cases in all. Of these, 31 were treated by radical operation, 8 by non-radical operations, 18 conservatively and 6 by osteotomy. The general and hygienic treatment was a very important factor. Under local treatment, he recommends the following: The mild cases are to be treated conservatively, as this is most likely to result in good healing. Rest and extension were especially favorable. But if complications arise, as suppuration, or if the conservative treatment is ineffective, operation should not be delayed any longer. The prognosis of operation depends much on the general condition of the patient. Garré operated only when life was in danger. Radical operations give good results with localized bone foci and sequestra. He advises against early operations because they are always very serious. They may lead to much shortening and increased lameness from injury to the bone without involvement of the epiphyseal line. The functional results from operative and conservative treatment are about the same, but after operation the shortening is greater. The results are not good from cutting and curetting fistulæ and abscesses without removal of the bone foci. Osteotomy for ankylosis gives good results and the danger of operation is about nil. It is difficult to say whether a movable or stiff joint should be striven for. A movable joint is most serviceable, but it must be used carefully. Therefore, the patient must be intelligent and under the control of a physician a long time. Ankylosis is less ideal but gives a good result for a working man.

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**A Case of Appendicitis with Ileocecal Intussusception.**—LEDDERHOSE (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 360) reports the following interesting case: A twenty-one year old under-officer was seized on the field with intestinal colic and dysentery and was taken to the hospital. The pain and straining movements of the bowels continued periodically and were associated with transitory abdominal tenderness and muscular rigidity in the right lower abdomen. Four weeks after the beginning of the trouble he developed the signs of acute appendicitis on account of which he was promptly operated on. The appendix was

the size of the thumb, brownish-red and tightly drawn from above downward. It passed through a sharp ring in the wall of the ascending colon and mesocolon. By careful pulling on the visible portion of the appendix it was gradually withdrawn and this was followed by the invaginated wall of the lowermost portion of the cecum and ileum. By this time the ring had disappeared. The appendix showed a strangulated ring but the cecum and ileum showed no signs of strangulation or stasis. The extirpated appendix showed subserous miliary pus foci and was tensely filled with pus. The mucus membrane was partly neurotic and the wall was nearly perforated at several places. Good healing followed the operation. Ledderhose believed the case one of chronic ileocecal invagination with acute appendicitis. Whether a causal relationship existed between intussusception and the appendicitis could not be decided.

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**Decapsulation of the Kidney for Bichloride of Mercury Poisoning.**—LUXEMBOURG (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 377) calls attention to Kummell's case in which the decapsulation of the right kidney for a complete anuria of seven days' duration, due to a severe poisoning, was followed in a few hours by the passage of 500 c.c. of urine and a larger quantity later. When the patient died eighteen hours after operation, she had passed over a liter of urine. Luxembourg reports four cases operated on by the late Professor Bardenheuer, of severe bichloride poisoning with good results. Tisseraud-Besancon operated on 3 cases of quicksilver poisoning with good results. Luxembourg concludes that in acute quicksilver poisoning, decapsulation of the kidney is a simple and not dangerous operation. As a consequence of the operation, the urine is again secreted. The decapsulation should be undertaken in all toxic nephrites from poison taken by the mouth and stomach, as soon as possible after the anuria has begun.

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**The Results of Eighty Pyelographies.**—PLOTKIN (*Jour. d'urolog.*, 1915, vi, 431) says that pyelography or the study of the renal pelvis and ureter by means of roentgenographs after the injection of the ureter and pelvis with collargol solutions, has made possible the study of the pelvis, its various physiological anomalies and pathological changes. The beginning of a ptosis of the kidney is shown by the changed relation of the kidney to the last rib. A kink of the pelvis or a twist of the ureter is shown by the stagnation of the urine and the distention of the pelvis. In movable kidneys the calices preserve their normal form although distended, but when infection sets in the calices change. Pyelitis and pyelonephritis, due chiefly to the colon bacillus, cause dilatation of the calices and ulceration of the papillæ. Pyelography renders good services in disclosing congenital strictures of the ureter impassable to fine catheters and capable of causing hydro-nephrosis and severe colic simulating that of renal calculus. It is not of great importance in pronounced hydro- and pyonephrosis, because these conditions can be easily diagnosed by the clinical methods and the functional tests. It is valuable in the beginning of renal tuberculosis when the parenchyma is only mildly involved and the functional tests show nothing abnormal. It can show changes in the papillæ which habitually indicate the commencement of the tuberculous pro-

cess. In certain calculi permeable to the Roentgen-ray, the presence of the collargol cause a different shadow to appear at the site of the calculus. In the hands of experts, Plotkin considers that its use is without much danger. There is no more danger than in passing the ureteral catheter or lavage of the renal pelvis.

## THERAPEUTICS

UNDER THE CHARGE OF

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**Serum Treatment of Scarlet Fever.**—REISS and HERTZ (*München. Med. Wchnschr.*, 1915, lxii, 1177) report further favorable results from the intravenous injection of mixed serum from several scarlet fever convalescents in the treatment of scarlet fever. They advise the intravenous injection of at least 50 c.c. for children and 100 c.c. for adults. The injections should be given as early as possible in the disease—to secure the best results. The serum to be injected is obtained from the donors between the eighteenth and twenty-fourth day of their disease. The donors should have preliminary Wassermann tests and tuberculous and septic patients should be excluded as donors. Reis and Hertz have occasionally observed the same beneficial effect following the injection of ordinary human serum, as convalescent serum, but much less often and consequently the use of ordinary serum for therapeutic purposes is more unreliable. Normal horse serum seemed entirely without any effect. The indications for this form of serotherapy are the severer toxic forms of scarlet fever, especially those cases with restlessness, delirium or evidences of heart weakness. In cases of scarlet fever where the toxic symptoms are due to secondary infection, serotherapy has no marked effect.

**Treatment of Syphilis of the Brain.**—IRELAND and WILSON (*Jour. Amer. Med. Assn.*, 1915, lxy, 1108), using the method of Byrnes, found that the intradural injection  $\frac{1}{50}$  grain of mercury chloride in serum was safe. The reactions were a little more severe than following the Swift and Ellis method of 40 per cent. salvarsanized serum. They found that a clinical improvement usually appeared after about five treatments; 75 per cent. of their cases showed this improvement. A tendency to relapse to their former condition was observed in about 40 per cent. of those at first improved. They noted that clinical improvement was more marked and rapid than the serologic. Ireland and Wilson report a total of 23 cases with brief summaries of each case but note that their period of observation is too short to permit any definite conclusion regarding the permanency of benefit.

**The Use of Calcium in the Treatment of Epilepsy.**—BRYANT (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 547) writes concerning the results obtained by the use of calcium in the treatment of epilepsy. The calcium treatment was combined with the usual bromide treatment. The official syrup of calcium lactophosphate was used in doses of from one to two drams three times a day. Bryant believes that calcium, in favorable cases, promotes sleep, decreases nervous irritability, and acts in some measure as an antidote to bromine acne. Nearly all cases have shown some benefit, in some very striking improvement followed the treatment. Calcium is not presented by Bryant as a panacea. He says it may not cure any case, but it at least can be said that when added to existing only partly successful treatment by bromides, it has in some cases produced results sufficiently encouraging to make it seem desirable to mention its employment and possible value.

**The Clinical Type of Arthritis Originating about the Teeth.**—HARTZELL (*Jour. Amer. Med. Assn.*, 1915, lxv, 1093) has made bacteriological examinations of the teeth and peridental tissues in 220 patients suffering from arthritis. He has invariably found the *Streptococcus viridans* present not only in the confined dental abscess but also in the superficial tissues of the peridental membrane. The same results were obtained in the examination of the roots of normal lining teeth in a considerable series. Hartzell believes that the arthritis of dental origin is always due to a *Streptococcus viridans* infection. It is characterized by slow onset with more or less frequent exacerbations and remissions, which exacerbations seem coincident with the filling to distention of dental abscesses or retention of pus from deep pyorrhea pockets, which drain slowly into the circulation. Exacerbation frequently follows surgical treatment of pyorrhea or the curettage of alveolar abscesses. Treatment of pyorrhea pockets by curettage and evacuation of dental abscesses confers a double benefit. Such surgical interference necessarily inoculates the patient with a large number of organisms, inducing an effect similar to that of an efficient vaccine, with the added advantage that the constant supply is shut off from the focus disturbed. When many pyorrhea pockets or abscesses exist, it is important to permit from three to six days to intervene between treatments in order to gain the full advantage of what might be called surgical auto-inoculation. Certain it is that the above method brings about a constant and permanent gain generally ending in cure, whereas, if sudden complete extirpation of all foci is practiced as, for example, extraction of all the teeth at once, as is done in some instances, or extraction of all the teeth and removal of tonsils on the same day, the end-result will be positive harm. This type of arthritis is easily controlled when of dental origin, if the foci of infection are early recognized and eliminated. When, however, such foci obtain in an active state for a considerable period of time the disease becomes so firmly fixed that elimination of the primary focus does little in the way of repair, though elimination does limit further progress of the disease.

**On the Treatment of Exophthalmic Goitre Especially in Relation to the Control of Protein Metabolism.**—BOYD (*Edinburgh Med. Jour.*, 1915, xv, 108), after speaking briefly of general dietetic and hygienic

measures in the treatment of exophthalmic goitre says he has never been able to convince himself of any benefit following the use of belladonna. The same seems to apply to digitatis, strophanthus, and other cardiac tonics. The deleterious effects of iodide of potash or thyroid extract in Graves' disease are in most cases so pronounced and definite that in early cases when the diagnosis may be doubtful, their administration has been advocated as a means of establishing a diagnosis. The treatment of Graves' disease by preparations of the milk or blood of thyroidectomized sheep have not, in Boyd's experience, given satisfactory results. Boyd emphasizes particularly various measures to influence the excessive protein metabolism in exophthalmic goitre. He has found that extract of the whole adrenal gland has a certain definite influence in restraining the increased protein metabolism. The influence of parathyroid extract is but small and the impossibility of obtaining a reliable extract commercially precludes its clinical use. Radium is always useful but its general application is difficult and impossible in many cases. Treatment by Roentgen-rays is simple and often very effectual. A daily application for a week is followed in most cases by definite amelioration of symptoms. Excessive protein metabolism is restrained and the patient gains weight. The treatment can be repeated at the end of a month or six weeks.

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**The Treatment of High Blood-pressure.**—STRAUSS (*Therap. Monatsh.* 1915, xxix, 10) says that it is important to distinguish between simple and complicated blood-pressure. He defines the latter as hypertension associated with subjective symptoms. In the cases of hypertension associated with sclerotic kidneys, the high blood-pressure seems to be compensatory and together with hypertrophy of the heart is necessary to enable the kidneys to excrete the increased amount of urine. In such cases the aim of treatment is to protect the patient from useless overstrain of the heart and to guard against cerebral hemorrhage. Strauss warns against dietetic excesses, severe physical exertion and mental excitement or unrest as causative factors in hypertension. He advises elimination from the diet of all alcoholic stimulants, coffee, meat extractives, etc. With regard to medication Strauss states that small doses of digitalis, not over 0.1 gm. per day, are very useful and harmless in arteriosclerosis with high blood-pressure and beginning cardiac insufficiency. He has kept digitalis medication up for years with some of his patients, alternating two weeks of these small doses of digitalis with two weeks of iodine. The combination of a number of measures such as can be best carried out in a sanatorium—diet, baths, graduated exercises, etc., are especially beneficial in hypertension.

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**The Treatment of Paresis.**—READ (*New York Med. Jour.*, 1915, cii, 561) has treated 20 cases of patients with 123 intralumbar injections of neosalvarsan, in doses ranging from 0.003 to 0.006 gm. diluted in at least 10 c.c. of the patient's own spinal fluid. During the treatment three patients died, but of these two were in the final stages and the deaths could not be fairly attributed to the treatment. One case, already slightly spastic when received, became intensely spastic and died with symptoms of motor tract degeneration. Two patients suffered incontinence. A few complained of weakness, headache and leg

pains from time to time after treatment. One case developed a Charcot joint during treatment. One patient had convulsions following a treatment, but has had others not connected with the treatment. The Wassermann of the blood serum in 9 cases remained 4 plus. In two cases it is now negative, but in one it was negative before treatment and in the other it was not tested. One negative and one faintly positive Wassermann reaction in the spinal fluid have become strongly positive. The above are the unfavorable results. The favorable results are the following: One case has entered a fair remission but still shows positive fluid findings. Another is improved markedly, but is still very evidently paretic. A number show improved conduct or physical health which may possibly be the result of hospital care. In 3 cases the Wassermann in the spinal fluid has become weaker. From the foregoing results Read concludes that the intralumbar treatment with neosalvarsan in smaller quantities is without effect and that when pushed with the object of obtaining results, it is extremely apt to prove injurious. Its use in this manner is to be discouraged.

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**The Use of Convalescent and Normal Blood in the Treatment of Scarlet Fever.**—ZUGHIER (*Jour. Amer. Med. Assoc.*, 1915, lxy, 875) reports the results obtained in treating twenty-three scarlet fever patients at the Willard Parker Hospital with intramuscular injections of blood. This group of patients represent the cases with the poorest prognosis, selected out of a total of some nine hundred admissions. Fifteen were treated with convalescent blood, which was citrated in a majority of cases. Nine received blood from two or more donors. The amount injected varied from 2½ to 8 ounces. Of the fifteen patients, four died; of these (a) one died from septic bronchopneumonia two days after the injection; (b) one died of a streptococcus sepsis nine days after the injection; (c) one was moribund when injected intravenously. He seemed to rally slightly, but the treatment was evidently given at a time when the patient's nervous system was entirely overwhelmed by the toxemia; (d) the fourth patient, practically moribund at time of injection, had severe meningismus with a marked retraction of the head; he died thirty-six hours after injection. Of the eleven patients who recovered only five were of the purely toxic type; the remaining six patients had additional severe septic complications, especially tonsillar and faucial exudates, and inflamed cervical glands. The five purely toxic cases showed a critical drop in temperature which varied from 3° to 6° F., after which the temperature remained normal or slightly above normal. In the remaining six cases, the drop in temperature was less marked and was followed by a secondary rise which persisted for a number of days. These secondary temperatures were evidently due to the septic complications. Eight patients received fresh normal blood; of this group, none died. These cases were far advanced septic cases, several with a poor prognosis. The blood, which was readily obtained from one or both of the parents, was citrated in six. One of the patients received two injections of 6 ounces each; another three injections, each of 8 ounces at intervals of four or five days. As was to be expected, no striking critical drop but a distinct lowering of the temperature curve was noted, associated with an improvement in the septic complications and the general condition

of the patient. The good results in some of these cases are the best proof of the beneficial effect that can be derived from this treatment. While it is difficult to make any absolute statement or arrive at definite deductions from such a small series of cases, one can only hope that, by continuing this form of treatment, a larger series of cases may finally be collected that will serve as a more definite guide for the value of the intramuscular injections of convalescent and normal blood. The treatment is easily carried out, is quite harmless, and is within the reach of the general practitioner. The beneficial effects noted in the above groups of very severe cases were quite distinct. The rational element in the use of convalescent blood is apparent, so long as the etiology of scarlet fever is not known, and the use of antistreptococcus serum during the past ten years has not given the striking results that were expected from it after the early trials. The rational element in the use of fresh normal blood in the septic cases is found, first of all, in clinical observations of its great empiric value; but also to a large extent, in a consideration of the great nutritive value of homologous blood, its marked stimulating properties, and its well-known antibody content which exerts a distinct bactericidal effect on many pathogenic organisms.

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**Fatalities after Salvarsan.**—FISCHER (*Deutsch. med. Wchnschr.*, 1915, xli, 908, 939, 976) summarizes his long serial article regarding the reported cases of fatalities following salvarsan as follows: The only injuries from salvarsan actually demonstrated at the present time are local necrosis at the point of the injection, and hemorrhagic encephalitis. Many accidents including death have followed salvarsan injections, but most have not been due to the medication. In a number of instances the fatal result has been determined by coincident disease. He cites as examples one case of generalized tuberculosis, with both suprarenal glands destroyed that died soon after salvarsan treatment; in a second case the fatal result seemed to be due to a coincident recent abortion and hemorrhage and in a third case an unsuspected pneumonia was found. Among the fatalities ascribed to salvarsan are cases in which no lesions, not even microscopic, could be found at autopsy and no evidence of toxic chemical action could be discovered. In one case chemical investigation revealed evidences of mercurial poisoning and Fischer believes that some of the fatal cases are probably more likely due to mercurial poisoning rather than to poisoning with salvarsan. He claims that there is no evidence that salvarsan has a toxic action on the liver cells. In those cases developing an acute yellow atrophy of the liver following salvarsan injections he believes that the degeneration of the liver is due directly to the virus of syphilis and not to the toxic action of salvarsan. The poisonous action of salvarsan does not correspond to the clinical picture of arsenic poisoning. He says that cases which appear to justify this conclusion have been imperfectly studied.

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**The Treatment of Syphilis with Salvarsan Alone.**—KREFTING (*Deutsch. med. Wchnschr.*, 1915, xli, 979) claims that mercury adds nothing to the efficacy of salvarsan in the treatment of syphilis. He believes that primary syphilis can almost certainly be cured with

from three to five injections of salvarsan at intervals of fourteen days. He advocates using large doses when treating early stages of syphilis. He says that definite rules for the salvarsan treatment of secondary syphilis cannot be made. The treatment must be individualized using the remedy in smaller doses than when treating primary syphilis. Salvarsan treatment should be used over prolonged periods of time and should be persisted in for some time after the Wassermann reaction becomes negative.

## PEDIATRICS

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**Mumps: A Critical Review.**—FEILING (*Quart. Jour. Med.*, 1915 viii, 255) states that this disease often belies its supposedly benign character as shown by recent advances in the knowledge, especially, of its complications and especially that of the nervous system. The disease may occur without acute inflammation of the parotid gland. The age incidence reaches its maximum between the fifth and fifteenth years, but no age is exempt. The mortality is extremely low. There is a prodromal stage before the appearance of the characteristic parotitis, during which infection is possible. This stage is probably four days long. The duration of the contagion is probably three weeks from the onset of the disease, although Sharp reports two cases remaining infectious for six weeks. The causal organism of mumps has not been satisfactorily isolated. Nicolle and Conseille by injecting fluid from parotid glands of patients with mumps into the parotid glands of monkeys apparently have demonstrated transmission of the disease, the occurrence of immunity following it and blood changes similar to those found in the human patient. No organisms were found. Gordon's experiments along similar lines with monkeys showed distinct changes in the nervous system such as lymphocytic infiltration and nerve cell degeneration. He concludes that mumps is apparently due to a filterable virus comparable to that of poliomyelitis, smallpox, and typhus; that the virus can pass through a Berkefeld filter and is destroyed at 55° C. Feiling gives the changes in the blood as a slight increase in the total number of leukocytes; a lymphocytosis both relative and absolute which persists from the first day for at least fourteen days. The occurrence of orchitis does not invariably alter the blood picture. The blood changes are of distinct value in differentiating mumps from other inflammatory swellings of the parotid or submaxillary salivary gland. The complications affecting more frequently adults are grouped as follows: Abnormal modes of onset, such as testicular involvement preceding the parotitis or meningeal symptoms ushering in the disease; orchitis followed frequently by atrophy; pancreatitis, the commonest cause of which, in children, is probably mumps; nervous symptoms,



including meningeal symptoms, rarely meningitis, and a marked lymphocytosis of the cerebrospinal fluid; lesions of the cranial and peripheral nerves including facial paralysis, herpetic eruption, and toxic polyneuritis.

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**Whole Milk in Artificial Feeding of Infants.**—Vining (*The Practitioner*, 1915, xcv, 589) makes a plea for the more frequent use of whole milk in artificial infant feeding and claims that the frequency of rickets is partly due to wrong methods of feeding, especially dilution in modified forms of feeding and the use of proprietary foods. He suggests whole milk feeding in all cases where the natural supply is not available. In discussing the usual objections to whole milk feeding the author claims that the difficulty in using whole milk lies in the mechanical factor of clot formation and that the use of heat (110°) or the addition of sodium citrate prevents clot formation and makes this form of feeding successful. The addition of sodium citrate has no effect of drugging as cow's milk normally contains sodium chloride and citric acid. The constipation met with in whole-milk feeding is not due to the sodium citrate as the same condition occurs in breast-fed infants. As to dried milk, the author claims that fresh milk may be sterilized by heating and if there is any risk of scurvy in either it would seem to lie in the use of dried milk. The dried milks, however, are superior to the proprietary foods. Babies can be fed successfully on whole milk containing sodium citrate from one to two grains to the ounce at any time after the first month. As to the amount to be used the best method is to allow the baby to indicate the amount it requires, the amount varying naturally at different feedings, and to check this by observing the condition of the stools, the amount of sleep, its weight and physical development. Constipation must be avoided and liquid paraffin or equal parts of the confections of sulphur and senna are recommended.

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**Radiography of the Thorax in Children.**—Fowler (*Edinburgh Med. Jour.*, 1915, xv, 326) offers a number of case histories to demonstrate the value of radiography of the chest in children for determining particularly tuberculous changes. The diagnosis of miliary tuberculosis in children is often difficult and frequently the radiograph shows lesions that show no clinical signs. The radiograph is, however, usually characteristic and affords probably the earliest means of making a correct diagnosis. One of the cited cases was a child of eleven years who ran a slight temperature, and lost weight four months after a serious pleurisy which could not be proven tuberculous. Physical signs showed no evidences of lung involvement, but a radiograph showed extensive miliary tuberculosis. Another case in a boy of five years was investigated by Roentgen-rays because a sister had had the disease. The boy showed no particular clinical signs and yet the radiograph showed a considerable mottling throughout the chest and a large shadow in the scapular region. He subsequently developed active tuberculosis and another radiograph showed quite an increase in the lesions. Exudates into the pleural cavity give a well-marked shadow. Fowler reports the case of a child of nine years with fever, headache and pain in the epigastrium which was not diagnosed for

some time when a radiograph showed a shadow over the left lung indicating pleurisy with lymph formation. From these facts gained from time to time the author places the radiograph very high in the diagnostic methods employed in conditions of the thorax in children.

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**Gastric Radioscopy in Children.**—WILLOX (*The Practitioner*, 1915, xcv, 599) gives a very minute and detailed account of his study of radioscopy on the stomach of the child. Every phase of the subject is discussed, the method, time, substance used, position of the child, etc. The objects were to determine the shape and general appearance of the stomach after a meal, the effect of different foodstuffs on motility, the rate of passage and the average time of emptying. From the author's summary of his investigation we find that the shape of the stomach with contents varies with the process of digestion, but that in general it is globular becoming elongated as the child ages, so that in older children immediately after a meal the stomach is of an "F" shape, resembling a Dutchman's wooden shoe. Foodstuff of itself has little if any effect on motility. Fluidity is the determining factor, the more fluid a meal is the more quickly will it pass through the stomach. Equal parts of milk and lime water pass more quickly than milk alone. Citrated milk goes through more quickly than plain milk. Stomachs of older children empty as quickly as those of younger children, provided the meal is similar in bulk and consistence. In some cases food begins to pass the pylorus as soon as the meal is taken, in some a resting stage occurs before peristalsis begins. The average time for the stomach to become empty was three and three-quarter hours. Porridge or bread and milk are the best media for either the barium sulphate or the bismuth, neither substance sets up intestinal disturbance. There is no evidence that bismuth forms a coating for intestinal mucous membrane. The stomach lies high up in the left hypochondrium in infants. The food passes the pylorus intermittently and in an apparently nodular form.

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**New Features in the Diagnosis of Scurvy.**—ALAN BROWN (*Arch. Pediat.*, 1915, xxxii, 741) in discussing the metabolism of scurvy points out some important features in the diagnosis of scurvy. The important points are fever, leukocytosis, great radiability of recently extravasated blood and the "white line." A high temperature and a leukocytosis, even as high as 26,000, occur in the severe and more advanced cases of scurvy where a faulty diagnosis of pus is apt to be made. The demonstration by Roentgen-rays of the "white line" is a valuable check to this diagnosis since the white line at the junction of the epiphysis and diaphysis occurs in scurvy even before the cardinal symptoms of the disease appear and represents an increased density at that point. The author has confirmed the findings of Talbot, that the "white line" is a constant sign of infantile scurvy that it may persist months after complete clinical cure and that it is of decided value in making an early diagnosis and instituting treatment. The production of this line is by hemorrhage between the diaphysis and epiphysis. The apparent difficulty at times of differentiating by Roentgen-rays between a recent subperiosteal hemorrhage and pus is caused by the greater radiability of recently extravasated blood over that which has already

begun to organize. The subperiosteal hemorrhage takes weeks or months to completely organize. In one of the author's cases complete absorption had not taken place at the end of five months. The absence of subperiosteal hemorrhage as shown by the Roentgen-rays does not therefore exclude scurvy. In scurvy fine petechial spots may usher in the prescorbutic stage. By applying a blood pressure cuff and 90 mm. of mercury minute petechiæ occur below the constriction in scorbutic patients (Hess). The "exudative diathesis" is associated so constantly with scurvy that Brown claims a close inter-relationship between the two and that the former implies a diathesis for the development of scurvy. The only etiological factor yet known in scurvy is diet and the most prominent foods are proprietary infant foods, condensed and sterilized milk. Scurvy is an exceedingly rare result of pasteurization. Sterilized milk, by the heating alone, causes a large number of cases.

## OBSTETRICS

UNDER THE CHARGE OF

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**The Use of Preparations of the Hypophysis in Obstetric Practice.**  
—VOGT (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) gives the results of his observations in the Dresden Clinic. He calls attention to the familiar facts that where the birth canal is dilated and dilatable, the position and presentation favorable, all that is needed is vigorous uterine contraction, that this substance will produce prompt uterine action and thus terminate labor. He draws attention to the fact that symptoms of threatened uterine rupture furnish a positive indication against its use. So do the symptoms and all indications of overdistension of the uterus. He mentions a case of transverse presentation with prolapse of the arm, where no diagnosis was made and pituitrin was given, followed by rupture of the uterus, which terminated fatally. Repeated doses do not seem to act in a cumulative manner; the drug can be repeated in from one to two hours during all the stages of labor. There are patients who bear it badly, in whom after the use of the drug, the pupils dilate, the pulse grows slow, there are symptoms of collapse, paleness, giddiness, prostration and cold sweat. If also the drug is given rapidly by intravenous injection in too large a dose, these symptoms may follow. In multiparæ, during the period of expulsion, the drug may cause very severe pains, which probably come from cramp-like contraction of the uterine muscle. This can be controlled by some preparation of opium, which does not seem to prolong the labor. The action of the drug may also cause formation of stricture and tetanus of the uterine muscle at the internal os. It would thus be a mistake to administer the drug before performing version or when it was necessary to dilate the lower portion of the uterus. In

some cases the uterine muscle seems exhausted by this preparation and atony of the uterus is observed afterward. The child's heart sounds are prolonged when pituitrin is given, and sometimes may be reduced to 80 or even 40 beats to the minute. The sounds are less distinct, the meconium is sometimes expelled, and the child may die from excessive pressure during birth. If pituitrin is to be employed the heart sounds should be carefully observed during the labor. These observations are based upon 7600 labors, with preparations of the hypophysis, manufactured by an American firm, an English firm, a French manufacturer and a German chemist.

**The Cause and Treatment of Transverse Position of the Fetal Head Complicating Labor.**—MARTIUS (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) reviews the literature of the subject and has gathered statistics and adds the results of his observations in the Clinic of Bonn. He thinks that great variations are present in the way in which the body of the child engages and passes through the pelvis. When the pelvic brim is a long oval and the head of the child corresponds to this peculiar formation, transverse position frequently develops. In some cases the elements which produce anterior rotation seem to be entirely lacking, the pelvis is without its normal contour, the head is rounded so that it does not fit the pelvis, and in some cases it is much smaller than the pelvis. In others the pelvis may be flattened, or the child may present by a parietal bone, and thus anterior rotation may be hindered. In five out of six cases, where no great disproportion exists between the head and the pelvis, labor will terminate spontaneously. It is best not to attempt anterior rotation by any manipulation, even though the pelvis should be somewhat abnormal. In flat pelvis, if the head permits considerable compression in the biparietal diameter, successful labor may still result. Where there is difficulty in the passage of the head through the pelvic brim, Walcher's position is especially valuable.

**Absorption from the Genital Tract during the Puerperal Period.**—AHLFELD (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) has conducted a long series of experiments to determine the question of absorption from the genital tract during the puerperal period. He concludes that at no time in pregnancy, labor or in the puerperal period does the absorption of material from the genital tract go on from the vagina and from the uterus at the same time. Independently of the size of the uterine cavity, absorption from the contracted uterus is diminished and from the relaxed uterus is increased. On the third, fourth, fifth and sixth days of the puerperal period absorption from the inner surface of the uterus reaches its highest point. As the uterus undergoes involution, from this time on the absorption steadily diminishes. When from any pathological condition the uterus remains greatly relaxed after the sixth day, absorption takes place with great freedom.

**Nephrectomy during Pregnancy.**—SCHMIDT (*Surg., Gynec. and Obst.*, December, 1915, reports the case of a multipara, aged twenty-eight years, who had renal infection with the B. colon and B. tuberculosis. The left kidney could be palpated as enlarged and sensitive. The patient was pregnant at about the end of the fifth month. The kidney

was removed through the usual incision, the ureter and vessels being separately ligated and the wound closed, except for both ends of the incision. The patient made a slow recovery, drainage persisting at the lower angle of the wound until after the childbirth. The patient had a normal labor but the baby died twelve days later of septic infection. On pathological examination the kidney was tuberculous with pyonephritis and ureteritis. Schmidt has in all collected 35 cases with a maternal mortality of two mothers (5.7 per cent.). In 77 per cent. labor was normal at term. In 15 per cent. the results of the operation were harmful upon the fetus. Three of these patients had spontaneous abortion: one induced abortion, one induced labor, one dead fetus extracted. As regards the time of operation, the greatest number of cases occurred in the fourth month of pregnancy; then in the fifth; then in the sixth. The remaining months had about the same number of cases. Especial attention must be given to the maintenance of function in the remaining kidney in a pregnant woman. Should this fail the uterus must immediately be emptied. The writer believes from a study of the subject that a woman with one absolutely healthy kidney and no constitutional infection may safely marry and incur the risks of pregnancy. He reports in detail the 35 cases collected and his own (36 in all). The reviewer recently had occasion to observe the patient admitted to the Maternity of the Jefferson Hospital suffering from eclampsia, one of whose kidneys had been removed for tuberculous infection. The patient recovered from the eclamptic seizure although the child succumbed. So far as could be ascertained, her recovery was complete and she reacted to treatment as well as other cases where both kidneys were present.

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**Premature Separation of the Normally Implanted Placenta.**—WILLIAMS (*Surg., Gynec. and Obst.*, November, 1915) in a paper on this subject states that in 2000 labors at the Johns Hopkins Hospital, antipartum hemorrhage was noted in 17 and placenta previa in 14 cases. As regards the cause of separation of the placenta, trauma is admitted; mental emotions have never been recognized, while a toxemic process is very frequently present. A change in the consistence of the uterus is a striking symptom. When the natural physiological alternation between contraction and relaxation is absent, the diagnosis is practically assured. The uterus remains hard and more or less painful and this condition is independent of concealed or external hemorrhage. An examination of the blood and the recognition of changes in the hemoglobin percentage will give valuable indications of danger, often before the pulse shows evidence of shock. Williams reports two cases treated by Cesarean section, with the recovery of the mothers. The children were dead at the time of operation. In the first case the uterus failed to contract and the operation was terminated with hysterectomy. A similar procedure was carried out in the second and, in both cases, a necrotic process in the muscular tissue of the uterus, described in 1911 by Couvelaire was demonstrable. While opinions may differ as to the precise pathology which examination of the specimens shows, in these cases there is clinical evidence of their association with a toxemic condition. Williams concludes that premature separation of the normally implanted placenta occurs more frequently than is

generally believed and may give rise to only trifling symptoms or may endanger the life of the patient. In severe cases the accident is associated with profound disorganization of the uterine muscle, by hemorrhage (called by some observers uteroplacental apoplexy). An undifferentiated form of toxemia is the probable cause and this may or may not be accompanied by albuminuria. As regards treatment, some cases terminate successfully spontaneously; in others labor must be induced and in others immediate operation is necessary. If the bleeding be but slight or the symptoms of separation be not pronounced, the patient may be put under observation, with the hope that nature will deal successfully with the case. If bleeding is profuse and the cervix admits easy dilatation or is already partially dilated, the use of a dilatation pack followed by forceps may be indicated. Where the cervix is but slightly dilated, abdominal Cesarean section is the operation of choice. Should hemorrhage occur after the uterus is emptied, it should be packed firmly with gauze and if this is unsuccessful the abdomen should be opened and hysterectomy done. So far as rupturing the membranes or tamponing the vagina is concerned, neither is advised. When the diagnosis of concealed accidental hemorrhage can be made Cesarean section is the operation of choice, except in the rare cases where the cervix is fully dilated and the conditions favorable for vaginal delivery. The reviewer has for some years treated such cases by abdominal Cesarean section with good results. He has twice performed hysterectomy for the condition described by Couvelaire and Williams. In one instance the placenta had been normally situated but separated and in the second a partial placenta previa was present. In both the mothers recovered but the children were dead at the time of operation.

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**Obstetrics — A Lost Art.** — HOLMES (*Surg., Gynec. and Obst.*, November, 1915) contributes a paper under this title, in which he criticizes the improper performance of Cesarean section. He argues that contracted pelvis alone is the definitely permanent indication for the operation; that the baby must be in good condition unless there is no other way of delivering safely, under any circumstances the fetal body. He would exclude eclampsia, placenta previa and believes that in the lesser grades of pelvic contraction the test of labor should be employed. Where the indication is absolute, labor should be avoided. Unless the patient be a multipara with a relaxed pelvic floor, a Cesarean section on one occasion would render necessary its performance for any subsequent pregnancy. He believes that the mortality of 5 or more per cent. for Cesarean section is too high. Many of the points in this paper are well taken but the experience of the reviewer does not coincide with the arguments advanced by the writer of the paper. We have repeatedly seen women who have previously had Cesarean section deliver themselves spontaneously and safely of living children. A mortality of 5 per cent. in clean cases is certainly excessive but if the desperate cases or sepsis and rupture of the uterus complicating contracted pelvis be considered, the mortality will inevitably be more than 5 per cent.

**Acute Inversion of the Puerperal Uterus.**—JASCHKE (*Zentralbl. f. Gynäk.*, 1915, xxxii) describes the case of a multipara, aged twenty-nine years, who had in one previous labor been delivered by forceps. The history stated that in four preceding pregnancies the placenta had to be removed manually at the time of labor. After her last pregnancy there was a severe hemorrhage on the twelfth day of the puerperal period. The patient was admitted to clinic two weeks before labor. She had varicose veins on the right thigh at the lower portion and the tissues of the thigh were considerably thickened. Labor proceeded rapidly and easily and a few moments after the expulsion of the child uterine hemorrhage occurred. The uterus was relaxed and Credé's method of placental delivery was employed in the effort to make the uterus contract. As the placenta did not separate it was removed by the hand and found to be adherent at the fundus and anterior wall of the uterus. On removing the hand without making traction upon the placenta and exercising the greatest possible gentleness, the uterus inverted itself completely. When the writer arrived, he found the uterus entirely inverted and outside the vulva and a portion of the placenta firmly adherent to the fundus. Hemorrhage had ceased with the inversion of the uterus. The patient was in severe collapse. Iodine was at once applied to the vulva as an antiseptic, the portion of placenta separated, the uterus replaced, when, upon withdrawing the fingers, the uterus again showed a tendency to inversion. This, however, was checked and the uterus tamponed firmly with gauze, when hemorrhage entirely ceased. Counter pressure was made by a firm abdominal bandage and a pad. In the puerperal period the patient had thrombosis of the veins of the right leg which could be traced to varicose veins on her side. The patient made a tedious but complete recovery.

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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**Cerebrospinal Meningitis and the Sphenoid Sinus.**—PETERS (*Jour. Laryngol., Rhinol., and Otol.*, July, 1915) and others report cases illustrating the intranasal conditions existent in cerebrospinal meningitis. As commented upon editorially Peters suggests that the sphenoidal sinus disease tends to lead on to meningitis if the orificial outlet of the sinus becomes blocked, and that therefore free drainage should be secured by the procedures familiar to the modern rhinologist.

**Buttermilk Gargle in Diphtheria.**—MOFFITT (*Pennsylvania Med. Jour.*, October, 1915) reports that in nine patients in whose throats diphtheritic bacteria remained after all other manifestations of the

disease had disappeared, buttermilk was used five or six times daily as a gargle. In eight of these cases an almost pure culture of lactic acid bacilli were found on the third day after beginning the procedure, no diphtheria bacilli being present. In the ninth case cultures on the fifth day showed a pure culture of lactic and bacilli.

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**Pharyngeal Fistula after Operation on Abscess in the Neck.**—HARMER (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports a glandular abscess which formed in the neck of a man shortly after a prostatectomy. Ten days after incision of the abscess there was paralysis of the palate with regurgitation of fluid through the nose, and soon afterward food passed from the mouth through the wound in the neck. As the abscess was not draining well the opening was enlarged. The wound in the neck and the suprapubic wound were both healing sluggishly at the date of the report.

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**Functional Aphonia following the Bursting of a Shell in Close Proximity to the Patient.**—TULLEY (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports two cases. The first one was that of a man, near whom a shell had burst on November 5 rendering him aphonic until December 11. The second case was that of a man who had been buried by a "Jack Johnson" for four hours. When dug out it was found that his voice had gone and likewise his hearing. He remained thus for three months and was sent into the hospital. In neither patient could any other morbid condition be found, while inquiry showed that the voice had been strong before the accidents. The first patient got well in response to a moderate intralaryngeal faradic shock. But even a strong faradic shock did not restore phonation in the second case. As the patient refused to open his mouth the laryngeal electrode was passed through the left nasal cavity into the larynx, and the current increased until the resulting spasm induced marked cyanosis. On removal of the electrode the patient's voice returned, and he spoke for the first time in three months. His hearing was also returned. These faculties had not been lost since, but the general condition might be described as that of profound neurasthenia. O'MALLEY (*Ibid.*) reports six cases of functional aphonia which had come under his own care, all having occurred in the trenches. In four the voice returned on asking the patient to phonate with the laryngoscopic mirror in position for the purpose of examination. In the other two a mild application of the faradic current proved effective. WHALE (*Ibid.*) reports a case of sudden aphonia in the trenches without any history of injury. The movements of the vocal cords were perfect, but there was cessation of expiration on their adduction. There was sudden recovery from the neurosis in twenty-four hours.

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**Malignant Tumor at the Base of Tongue almost Dispersed by Radium.**—HILL (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports the case of a male subject, fifty-five years of age, with a growth the size of a walnut ulcerating posteriorly, and with secondary involvement beneath the left angle of the jaw. The left side of the tongue was fixed. There was occasional hemorrhage, and in addition salivation, dysphagia, constant pain and insomnia. The treatment was by in-



sertion in two places of small, hollow, needle-like emanation apparatus of platinum 0.3 mm. in thickness, containing an initial charge equivalent to 40 mg. of radium bromide for twenty hours altogether. All symptoms had disappeared, and the tumor had become so reduced that it might easily be overlooked on superficial exploration.

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**Tuberculosis of the Frontal Sinus.**—THOMAS (*Jour. Amer. Med. Assn.*, July 24, 1915) in reporting two personal cases states that but five in all had been reported previously, and gives a synopsis of these cases. Four of the five terminated fatally, and the other one had remained well for seven months after operation. Of the reporter's cases one recovered after two operations and had remained well for more than two years. The other case had been subjected to extensive intranasal operation two years before Dr. Thomas was consulted. It is reported as a case of "tuberculous frontal sinusitis with osteomyelitis, epidural, subdural and cerebral abscesses, resulting in death, a necropsy being held."

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**Trichinosis Simulating Frontal Sinusitis.**—PRATT (*Jour. Amer. Med. Assn.*, October 9, 1915) reports three instances occurring in his practice during the past two years. He has not found mention of any similar cases after a very comprehensive search of the literature. Two cases were in females aged thirty-one and thirty-two years, respectively, but the age of the male patient is not stated. The diagnosis in all three cases rested on (1) edema of the lids with absence of edema elsewhere; (2) negative nasal findings referable to the accessory sinuses; (3) the history; and (4) the proportion of eosinophiles (22 per cent., 20 per cent., 6 per cent., and afterward 20 per cent., respectively). In all these the presenting symptom was pain in the region of the eye and frontal sinus.

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**Laryngeal Stenosis and Collateral Injuries from Shrapnel, Bullet, and Bayonet Wounds.**—A number of interesting cases were reported before the Laryngological Section of the Royal Society of Medicine (*Jour. of Laryngol., Rhinol., and Otol.*, October, 15) to which the reader must be referred for detail and discussion.

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**Glosso-laryngo-scapulo-pharyngeal Hemiplegia following Gunshot Wound Behind the Right Mastoid.**—COLLETT (*Ann. de Mal. de l'oreille, du larynx, du nez et du pharynx*, August, 1915) reports this case in much detail. He states in conclusion that a glance at the base of a cranium shows that this new type of associated laryngeal hemiplegia could be produced by a lesion barely a centimeter in diameter, localized in front of the occipital condyle in such a way as to involve the affected cranial nerves, passing through the posterior lacerum, anterior condyloid and carotid foramina.

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**Paralysis of the left Recurrent Laryngeal Nerve due to Mitral Stenosis.**—GUTTMAN (*The Larynscope*, August, 1915) reports this case in a woman, aged twenty-six years, who had suffered with rheumatism seven years previously. There was a marked difference between the two radial pulses. Fluoroscopic examination revealed a markedly

dilated pulmonary artery, which, by pressure against the recurrent laryngeal nerve and against the aorta itself, produced the laryngeal paralysis and diminished the blood supply to the left upper extremity.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Tuberculosis of the Female Genitalia in Childhood.**—GRAEFE (*Inaug. Dissert.*, Halle, 1914) had an opportunity of observing 19 cases in children and comes to the following conclusions: Tuberculosis of the genitalia is much less common in children than in adults, but when found, appears more frequently to fall between the ages of one to five and ten to fifteen. These tuberculous foci are secondary to older lesions in other parts of the body and arise through a hematogenous infection. It is more common in the tube and uterus and rare in the ovary, vagina and vulva. The tuberculous process begins in the mucous membranes of the tube and uterus and from here extends into neighboring parts. Progressive caseation is prone to occur while there is little attempt at healing. Most frequently the process spreads from other parts to the tube, although in some instances a simultaneous attack in several regions may occur. The secondary infection of the peritoneum from the tube is more frequent than the reverse. Primary tuberculosis in the vagina and vulva is very unusual.

**Bacteriological Study of Tuberculosis of the Lymph Glands in Children.**—MITCHELL (*Edinburgh Med. Jour.*, 1914, viii, 209) examined the cervical, bronchial and mesenteric lymph glands of 29 autopsies of children. Cultures were obtained in 12 cases, 8 of which gave the human type of tubercle bacillus and 4 the bovine type. Three of the latter infections also involved the meninges. The mesenteric glands were claimed to be the seat of origin of the disseminated infection. In two of the bovine infections, the cervical and bronchial glands were also diseased. Seven of the eight strains of the human type had their origin in the bronchial glands. On several occasions positive cultures were obtained from the tonsils. The cervical glands were furthermore examined in a series of 80 surgical operations. In 71 instances the

bovine bacillus and in 7 the human type was isolated. Moeller, who eight times isolated the tubercle bacillus from the sputum and lung tissue, found only the human type. In compiling the results of other authors he states that of 36 investigators 974 cases of tuberculosis of lung and bronchial glands were examined. Of these the human type was isolated 967 times, the bovine five times and both human and bovine twice.

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**The Relation of Tuberculosis to Various Cirrhoses.**—ALESSANDRO (*Internat. Centralbl. f. d. ges. Tuberk. Forsch.*, 1915, ix, 323) studied the changes occurring in various parenchymatous organs in relation to the connective-tissue stroma. He found that chronic tuberculosis was prone to induce a connective tissue increase in all organs, but that some were more intensely affected than others. The spleen showed the earliest and greatest fibrosis, while the liver, kidney and pancreas followed in order. The process was one whereby the normal stroma was diffusely increased accompanied by the development of an accessory reticulum throughout the tissue. These organic changes, he believes, are the direct result of toxic substances arising in a tuberculous focus. The poisons are of such character that they stimulate connective-tissue formation in each organ that is reached. The toxins are distributed by the blood stream.

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**Laboratory Infections with B. Typhi.**—KISSKALT (*Ztschr. f. Hygiene*, 1915, lxxx, 145) has brought together various cases of typhoid fever which have been acquired during work in laboratories. These cases include not only those that have appeared in literature but also those from continental laboratories with whom he has had personal correspondence. In all, the author has collected 60 cases, many of these were the result of the accidental infection of the mouth by pipette during Widal examinations. Others were obtained during the examination of feces or urine. Of these there were 6 fatal cases. In the majority of instances of accidental infection of the mouth which had knowingly taken place, disinfection, usually with alcohol, was tried. It would appear that the stock laboratory cultures still retained high virulency for man.

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**Changes in the Aorta in Children and their Relation to Arteriosclerosis.**—In spite of the numerous studies and animal experiments, the etiological factors of arteriosclerosis are not agreed upon. The influence of age and mechanical stress is no longer considered of as great importance as the more active agents of which infections are the most important. Experimental proof of the influence of bacteria has been brought forward by French and American investigators. Added to this, STUMPF (*Ziegler's Beiträge*, 1914, lix, 890) has studied the arteries of young children in which no evident arterial disease was recognized, but where the microscopic study demonstrated the beginning of damage in the arterial wall. The aortas of 84 children were examined. Evidence of fatty degeneration was present in 44 cases. Of these 44, 31 were suffering from chronic disease. Of 36 cases dying of acute infections, 12 showed definite arterial lesions. The chronic conditions associated with arterial degeneration were tuberculosis,

chronic suppurations and marasmus. The author believes that the influence of these chronic diseases upon the arterial wall is not directly through the toxins, but rather by the indirect action of the altered state of nutrition.

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**Primary Cancer of Liver in Two Sisters.**—A considerable literature is available indicating the familial occurrence of cancer. To a certain extent, the occurrence of cancer in several members of a family represents chance findings particularly when the cancerous processes differ in their kind and location. It is rather striking, however, to have two individuals in the same family die of cancer of the same organ. HEDINGER (*Centralbl. f. Path.*, 1915, xxvi, p. 385) reports a primary cancer of the liver in two sisters. These came to autopsy within a week of each other. The first was aged seventy-one years, in whom the liver weighed 3900 grams. The left lobe of the liver was, for the most part, occupied by tumor masses with a small secondary in the right lung. Otherwise there were no metastases. The other sister was seventy-seven years old; the liver weighed 1980 grams and showed a white, cancerous tumor mass in the left lobe. Metastases were not present. In the second case the tumor did not seriously affect the health, but the patient died of heart disease. Cirrhosis was not present in either case.

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**The Development of Arteriosclerosis in the Aorta of Rabbits.**—The Russian School of investigators have introduced a new method of producing experimental arterial lesions which they claim simulate the human type. These have been obtained by the feeding of cholesterol. ANITSCHKOW (*Ziegler's Beiträge*, 1914, lix, 356) criticizes the previous work in that although lesions comparable to those in man were obtained, the conditions of the experiments were very artificial. In the present work he found that by feeding pure cholesterol, positive results were obtained at the end of a month. Furthermore by increasing the blood-pressure he was able to get equal arterial changes with less cholesterol and in a shorter time. Thus moderate increase in blood-pressure and slight rise in the blood cholesterol is of great importance. The use of adrenalin and cholesterol leads to a fatty deposit in the arterial wall quite different from the commonly found adrenal necrosis. Likewise, the suspension of rabbits by the hind limbs with the exhibition of cholesterol lead to similar fatty deposits. In some instances he observed the simultaneous occurrence of hyperplasia, degeneration and cellular infiltration of the arterial wall. The author believes that the results of his experiments can be directly applied to the interpretation of the human disease.

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ORIGINAL ARTICLES

MANAGEMENT OF PATIENTS WITH CHRONIC RENAL  
DISEASE.<sup>1</sup>

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It needs only a glance at current medical periodicals to show the amount of time and energy being devoted to the study of kidney function today. In fact, some may have been inclined to believe that the 'phthalein test and the electrocardiograph are the only methods now employed in the investigation of patients in our hospitals. So much work may surely, by this time, be expected to have produced some results which the practitioner of medicine can use for the good of his patients. It has been my fortune during this period of the development of functional tests, both at the Presbyterian Hospital, New York, and during the last year at the Johns Hopkins Hospital, to have for my associates a group of men actively interested in this field. During the last year, especially, Dr. Mosenthal and Dr. Rowntree and their co-workers in our clinic have, by their laboratory studies, quite definitely modified our practice in the wards. I shall give our present views on the practical management of the different types of chronic renal disease which are commonly met in general practice. I say "practical management of the patient," because, except in the rarest instances, we have no real treatment of the disease. We

<sup>1</sup> Read before the Academy of Medicine, New York City, November 4, 1915.  
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must not let the fascination of growing insight into the complexities of function blind us to the fact that the problem of fundamental importance in any disease is the problem of its cause. It is devoutly to be hoped that our knowledge may be increased along this line. The study of the relation of focal infections to renal disease is a promising movement, but a vast material must be worked over critically before we can reach conclusions. Except for certain cases of renal involvement in secondary syphilis, possibly rare cases of nephritis due to malaria, lead poisoning, pregnancy, or some focus of streptococcus infection, we can not speak of an effective causal therapy of chronic nephritis.

For the most part, treatment has in the past been purely schematic and based on a conventional diagnosis. Since this treatment usually involved violent interference with the habits of a lifetime, even though it did not use dangerous drugs, we can not regard it as a harmless procedure. To tell every patient with albuminuria or hypertension to stop eating red meat, or still worse, as I have actually seen done, to go on a milk diet, is evidence either of colossal ignorance or of inexcusable mental laziness. Nothing is clearer to me, however, in dealing with patients who have a chronic disease than the amount of thought and tact necessary to accomplish the readjustment of their life to the necessary limitations which they must be taught to recognize. This is a field which the internist has to himself, and it should be our pride to develop it in detail as carefully as the surgeon has developed his operative technic. Here is where the functional test becomes indispensable.

The treatment of chronic disease has two aims: the prolongation of life, and the amelioration of the discomforts due to the disease. These two aims are achieved by two types of treatment: (1) safeguarding treatment, which aims to protect a weakened function from further damage by overstrain; (2) symptomatic treatment, directed toward the amelioration of the symptoms which depend upon disordered function. While a correct anatomical diagnosis is always desirable it is not of special importance in determining treatment along either of these lines. What is fundamental is the accurate estimation of the kind and degree of functional damage.

Chronic renal disease presents an endless variety of symptom combinations, but certain clinical types occur with such frequency that we are all called on to meet the problem of their management; and they present themselves, in a way, as specific practical problems. I propose to consider them as such:

1. Patients in whom albumin and casts in the urine are the only evidence of disease. This is a large group. These patients come to us, both family practitioners and consultants, from the life insurance examiners; or if we have careful patients, and are careful examiners, we discover them among our supposedly healthy clients. They are found among the children in the clinics. Their problem is the

last problem we have to work out in a convalescent from known acute nephritis or from a pregnancy albuminuria. The last two instances give the key to the important question that must be answered for every patient in this group, namely, Are the albumin and casts in the urine the last remaining evidences of a healing renal lesion? A searching inquiry must be made into the history for evidences of a mild unrecognized scarlet fever, a tonsillitis, or other infection, recent pregnancy, syphilis, the administration of salvarsan, or some intoxication which might have led to acute renal disease without noticeable symptoms. If such possible cause can be found, or even suspected, especially in the case of young people, then a period of rest in bed and milk or bland diet should be given a thorough trial. If treatment, as of true acute nephritis, results in steady subsidence of the albuminuria, then it should be persisted in just as though the patient had a known acute nephritis. No sacrifice is too great for any patient to make which may prevent the subsequent development of chronic diffuse nephritis, leading to the secondary contracted kidney in later life. If, however, there is no suspicion of a past or existing infection, and if a week in bed on milk diet has no appreciable effect upon the albumin and casts, then bed and milk diet are an unwarrantable hardship, because they are sacrifice without result. If persisted in, the result will very likely be the sacrifice of the physician.

In children the next problem is the differentiation of postural albuminuria. This is much commoner than is usually supposed, and marked albuminuria without casts, or with rare casts, in a child should always suggest the possibility of its being this peculiar type. For an excellent discussion of this subject I can recommend the article by Langstein in *Pfaundler and Schlossman's Handbuch*,<sup>2</sup> for interesting special pleading on the two sides of the question, the monographs of Politzer and of Jehle.<sup>3</sup>

Testing the separate urines passed at different times of day, and the effect of standing fifteen to thirty minutes in marked lordotic position, will often clear up the diagnosis promptly. The large amount of protein precipitable by acetic acid in the cold has been, in my experience, an important feature of the albuminous urine in these cases. The treatment of these children should, I believe, be along the lines of general invigoration, with medical gymnastics for the improvement of posture. Their diet should be ample, not restricted. In some the suspicion of true nephritis is strong, though there is marked postural albuminuria. Such cases should be more cautiously handled.

<sup>2</sup> Langstein, L., Die orthotische Albuminurie, Handbuch, Pfaundler und Schlossman, 1910, iv, 30. F. C. W. Vogel, Leipzig.

<sup>3</sup> Ren juvenum, Beiträge zur Kenntnis der orthostatischen Albuminurie, Berlin und Wien, 1913, Urban und Schwarzenburg; Die Albuminurie, Julius Springer, Berlin, 1914.

When one has clearly recognized and separated from the patients in whom albuminuria has been accidentally discovered these two preceding types, residual albuminuria after acute nephritis and postural albuminuria, there remain the large number of patients in whom the cause of the albuminuria is not evident. In them it is of first importance to exclude inflammation of the urinary tract, stone, tumors, and other non-nephritic causes of albuminuria, the treatment of which is local and surgical. Then the search must be made for a remote focus of infection in tonsils, sinuses about the teeth, in the gall-bladder, in the prostate or seminal vesicles, and any such focus should be eradicated in the hope that from it as a portal of entry has come the infection responsible for the renal damage. Possible toxic causes, especially the inorganic poisons, should be in mind. I have seen albuminuria produced by the therapeutic use of arsenic for instance. In childhood and adolescence, albuminuria without casts and not definitely postural may exist without subsequent evidence of any serious injury to the kidney, and may be more lightly regarded than albuminuria in adult life.

The effect of exercise, cold baths, and so on upon the albuminuria should be studied. I have the records of one patient, who more than thirty years ago, was refused life insurance because of large numbers of hyaline casts in the urine. He came to my father, who discovered that life insurance examinations had always been made in the afternoon, after he had done some lively boxing, and had a cold shower. His urine was perfectly normal at all other times. Twenty-six years afterward he was still free from evidence of chronic nephritis, and, I believe, is still living. Such a patient either needed no advice at all, or to be told to avoid the combination of very active exercise and a cold bath. If exercise produces marked albuminuria with casts it should certainly be reduced.

Apart from wholly temporary albuminuria, however, it is wise for the physician to consider albumin and casts as the evidence of a definite renal lesion, to be watched over long periods of time in the interest of both science and the patient, but not necessarily calling for either a bad prognosis or much interference with the patient's life. Barringer's<sup>1</sup> studies of life insurance statistics show that the persistent presence of granular casts indicates a higher probability of progressive renal disease. Even so, these individuals may enjoy apparently perfect health for ten years or more. It is even more important to watch their blood-pressure than their urine. If this begins to rise, then the development of symptoms is to be looked for. A tendency toward nocturnal polyuria or to fixation of specific gravity is an almost certain danger sign. These point to beginning inability of the kidney to concentrate urea, and therefore connote

<sup>1</sup>The Prognosis of Albuminuria with or without Casts, *Arch. Int. Med.*, 1912, ix, 657-661.



anatomical damage which has reached the stage of seriously compromising the large factor of safety of the kidneys. Until hypertension, nocturnal polyuria, or other symptoms arise, symptomatic treatment is quite unnecessary. Safeguarding treatment is important, but must not go beyond what is of proved efficacy.

Severe physical strain, such as competitive athletics, rough hunting trips and so on, should clearly be avoided. Exposure to cold and wet is also unwise. The wearing of woolen underwear has long been regarded as desirable. Alcoholic and other excesses should naturally be warned against, also the immoderate use of tobacco. The common mild infections, such as tonsillitis, should be much more carefully treated than in normal individuals and the effect on the urine carefully observed.

As to diet, von Noorden<sup>5</sup> has shown that considerable quantities of pepper, mustard, and other condiments are renal irritants. He always held that creatinin was dangerous, and recent work, well summed up and amplified by Myers and Lough,<sup>6</sup> has proved that creatinin retention may be very striking in severe nephritis. Therefore, soups, which are unimportant as sources of energy, and spices may wisely be excluded from the diet. Gourmands should clearly have their excessive appetite restrained, and obese patients should be moderately reduced. If the 'phthalein test is normal I see no reason for a restriction of protein, either qualitatively or quantitatively, below a moderate normal intake. One limitation not immediately necessary, I believe, should be made for the sake of training the patient in case it may become imperative later. Patients who regularly use a large amount of salt with their food—that is the people who habitually put salt on before they have tasted the dish—should be told to reduce their use of added salt at table to foods which come from the kitchen unsalted. Without this training, treatment of subsequent edema in them will meet with serious obstacles. One special category under this heading comprises the diabetics with albuminuria. For them, unless the 'phthalein test shows an excretion below 40 per cent., or there are definite symptoms, such as edema, the treatment is the dietetic treatment of diabetes and the albuminuria should not be allowed to interfere with this.

2. Patients with hypertension, with or without a trace of albumin, and with slight subjective symptoms or none at all. These patients we all recognize at a glance. Since the introduction of blood-pressure measurements into practice they have come into prominence, often, from the stand-point of their comfort, an undesirable prominence. They are usually past middle age. Many of them

<sup>5</sup> Clinical Treatises on the Pathology and Therapy of Disorders of Metabolism and Nutrition—Nephritis, New York, 1903.

<sup>6</sup> The Creatinin of the Blood in Nephritis: Its Diagnostic Value, Arch. Int. Med., 1915, xvi, 536.

are obese, many diabetic. The functional disturbance is so clear-cut, and the anatomical basis in their arterioles so remote from observation, that we usually classify them under the functional category of hypertension. The vast majority certainly have changes in their renal vessels and in the arterioles elsewhere; but the clinical type which I have in mind here does not have renal symptoms. The development of nocturnal polyuria, of severe headaches, especially explosive headaches with vomiting; in patients who have not been subject to migraine, of retinal lesions, or of edema, takes the patient immediately out of this category. Slight cardiac or neurasthenic symptoms are common. Safeguarding treatment is the entire problem of their management. In the first rank must come safeguarding from all avoidable influences which raise blood-pressure in the normal man; next, safeguarding the myocardium and, to a certain extent, the cerebral vessels and the kidneys. The worst hypertensive influence is mental strain, and especially emotional strain. Its avoidance necessarily calls for readjustment of the every-day life for the man in business or for the woman in the home, and the details of this should be worked out with care and sympathy. Distinctly the worst advice is to tell a man of important affairs to give up business completely; but for the manual laborer change of occupation may be imperative. It is of great importance to secure adequate normal sleep. In addition, I believe that the strain of a hard day's work can be greatly reduced by a short break in the middle of the day for absolute rest, or, better yet, for a little exercise, followed by rest. With more marked myocardial symptoms a few days in bed will work wonders, often reducing blood-pressure greatly. Tobacco in excess is clearly a poison both to vessels and to cardiac mechanism. Whether two or three mild cigars a day may be smoked while the patient is sitting quietly after meals must be determined in the individual case. Their effect upon blood-pressure should be observed. If the patient is perfectly miserable without them it may wisely influence the physician. Excessive athletics may be dangerous to both heart and vessels, but I believe that, as a rule, these patients may take more exercise than is usually allowed them— even women who have not previously been accustomed to it. The functional response of the myocardium is the determining factor, and can often be improved by proper exercise. Slight dyspnea on exertion may become less or disappear with gradual training. Mild anginoid pain on exertion, however, calls for great care, and the patient should always stop when it is felt. When exercise cannot be allowed, massage is helpful. The reduction of obesity is a highly important measure. Limitation of diet follows much the same lines as in the preceding class of patients, but physiological economy in nutrition should usually be insisted on, and meals should not be bulky. Moderation in the use of salt, I think, is quite important. The abuse of fluid is clearly dangerous

for them, as von Noorden has insisted. High blood-pressure is no indication of nitrogen retention, as Folin, Denis, and Seymour<sup>7</sup> have shown, and protein should not be restricted merely because of hypertension. Luxur consumption clearly should be, and it is possible that some patients will be, better without meat. On the other hand I am sure that others may be made worse by the loss of appetite that an unpalatable diet produces.

Alcoholic drinks are condemned by von Noorden in these patients. I am not convinced that every patient who has taken wine temperately all his life should be deprived of it absolutely. One should judge by its effects on the circulation. If it causes marked flushing of the face or palpitation it should clearly be avoided; but if it leads to greater enjoyment of meals and to relaxation after it may be permitted. It is needless to say that it should be used sparingly and in dilute form.

Climate has seemed to me not without its influence. The majority of these patients have more symptoms during cold weather, and the combination of cold and high wind taxes the heart maximally. For those who live in the North a winter vacation in a warm climate is desirable. For all of them a long break in their work once or twice a year is most helpful. Turkish baths or other sweating procedures benefit some. Vasodilators should not be used except in emergencies, and aconite, I believe, is worthless.

3. Patients with hypertension and outspoken myocardial insufficiency. This is one of the largest groups to be found in the medical wards of every hospital, and these patients are equally common in private practice. They present primarily the problem of treatment of a circulatory disease. For them both safeguarding and symptomatic treatment are essential. The symptoms demanding treatment in the majority are dyspnea, edema, and the whole picture of cardiac failure with chronic passive congestion of the viscera. A small number have anginoid pain on exertion or severer attacks of angina pectoris. For the latter the essential safeguarding treatment is rest, never permitting enough exercise to produce an attack. Symptomatic treatment consists in the use of vasodilators to cut short or to ward off an attack when exertion must be made. Fresh nitroglycerin tablets dissolved on the tongue and not swallowed have always fulfilled the indications in my experience, and are free from the disagreeable publicity which the breaking of an amyl nitrite pearl entails. Vasodilators have their most important use in these people, who owe Lauder Brunton a great debt of gratitude for the introduction of the nitrites into medicine. Theobromine may be valuable in some cases. It is not necessary for me to go into the treatment of angina in further detail.

<sup>7</sup> The Non-protein Nitrogenous Constituents of the Blood in Chronic Vascular Nephritis (Arteriosclerosis) as Influenced by the Level of Protein Metabolism, *Arch. Int. Med.*, 1913, xiii, 224.

The patients with ordinary myocardial failure do not present a simple problem of circulatory therapeutics. Their study by the nephritic test meal, originally advocated by Schlayer and Hedinger, and which Mosenthal<sup>8</sup> has adapted and amplified with such excellent results in our clinic, has shown the importance of the special functional changes, depending upon chronic passive congestion of the kidney in retaining salt, and thus in producing at least the edema if not other symptoms of the disease. Every case of this type should, I believe, be given such a test, and should have a phenolsulphonephthalein test as a preliminary to treatment. If, in addition, the blood urea and the Ambard coefficient can be determined, very valuable information may be gained. The 'phthalein output is usually low, often under 30 per cent., sometimes minimal. If normal, or nearly so, and the test meal shows no lowering of the nitrogen concentration in the urine and no marked nitrogen lag, then it is rarely necessary to determine the blood nitrogen. Only in moribund patients can important retention exist. It is also essential to recognize the presence or absence of fibrillation of the auricles as a guide to the use of digitalis. Clark's<sup>9</sup> study of venous pressure in our wards, using Hooker's simple method, has also given us valuable indications of the need for digitalis.

All these patients require rest in bed, or in a chair if they are orthopneic, as the essential safeguarding treatment for the heart. Those with auricular fibrillation must receive effective digitalis treatment. Choice of the preparation and the method of administration, as between strophanthin intravenously or intramuscularly, infusion or tincture of digitalis, the powdered leaf of *digipuratum*, being determined by the details of the case and the habits of the physician. Those without auricular fibrillation, but with marked edema and a congested liver, should, I believe, also be placed on digitalis. Many of them will respond as well as the fibrillating cases; others will not. Toxic effects must be watched for and heeded, as some patients with regular rhythm are made worse by digitalis. If it does not succeed alone with proper diet, then one of the caffein diuretics—*theocin*, about twelve grains a day, or *diuretin*, about forty grains, in divided doses—should be given not oftener than every other day. It is very important to have the fluid intake and urine output accurately measured, and it is helpful to have the daily weight recorded. Diuresis from digitalis by the ordinary administration by mouth should not be expected before forty-eight hours. The diuresis of the caffein group of drugs, however, should be observed on the chart of the day of administration, and may

<sup>8</sup> Renal Function as Measured by the Elimination of Fluids, Salt, and Nitrogen, and the Specific Gravity of the Urine, *Arch. Int. Med.*, 1915, xvi, 733.

<sup>9</sup> A Study of the Diagnostic and Prognostic Significance of Venous Pressure Observations in Cardiac Disease, *Arch. Int. Med.*, 1915, xvi, 587.

then persist for one or two days longer. The next doses should be given when the diuresis ceases.

## NEPHRITIC TEST DIET.

For..... Date.....

All food is to be *salt-free* food from the diet kitchen.

Salt for each meal will be furnished in weighed amounts.

*All food or fluid not taken must be weighed or measured after meals and charted in the spaces below.*

*Allow no food or fluid of any kind except at meal times.*

Note any mishaps or irregularities that occur in giving the diet or collecting the specimens.

## Breakfast, 8 A.M.:

Boiled oatmeal, 100 gms.	.....
Sugar, 1 to 2 teaspoonfuls..	.....
Milk, 30 c.c.	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Coffee, 160 c.c.	.....
Sugar, 1 teaspoonful	} -200 c.c.
Milk, 40 c.c.	
Milk, 200 c.c.	
Water, 200 c.c.	.....

## Dinner, 12 Noon:

Meat soup, 180 c.c.	.....
Beefsteak, 100 gms..	.....
Potato (baked, mashed or boiled)	.....
130 gms.	.....
Green vegetables as desired	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Tea, 180 c.c.	} -200 c.c.
Sugar, 1 teaspoonful	
Milk, 20 c.c.	
Water, 250 c.c.	.....
Pudding (tapioca or rice), 110 gms.	.....

## Supper, 5 P.M.:

Two eggs cooked in any style	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Tea, 180 c.c.	} -200 c.c.
Sugar, 1 teaspoonful	
Milk, 20 c.c.	
Fruit (stewed or fresh), 1 portion.	.....
Water, 300 c.c.	.....

8 A.M. No food or fluid is to be given during the night or until 8 o'clock the next morning (after voiding), when the regular diet is resumed.

Patient is to empty bladder at 8 A.M., and at the end of each period, as indicated below. The specimens are to be collected for the following periods in properly labeled bottles, to be furnished by the chemical division of the medical clinic: 8 A.M. to 10 A.M.; 10 A.M. to 12 N.; 12 N. to 2 P.M.; 2 P.M. to 4 P.M.; 4 P.M. to 6 P.M.; 6 P.M. to 8 P.M.; 8 P.M. to 8 A.M.

Specimens are to be left in the ward until called for at 8.30 A.M. by an attendant from the chemical laboratory.

## REPORT ON NEPHRITIC TEST MEAL.

Name	Date						Time and c.c. of fluid intake.
Time of day	Cubic centimeters	Specific gravity.	NaCl. Per cent.	Grams.	Per cent.	N. Grams.	
8 to 10	153	1.016	1.32	2.02	.89	1.26	
10 to 12	156	1.019	1.25	1.95	.74	1.15	
12 to 2	194	1.012	.64	1.24	.59	1.14	
2 to 4	260	1.014	.77	2.00	.56	1.46	
4 to 6	114	1.020	.99	1.13	.95	1.08	
6 to 8	238	1.010	.43	1.02	.52	1.23	
Total day	1115	.....	.....	9.36	.....	7.32	
Night, 8 to 8	375	1.020	.63	2.36	1.23	4.61	
Total 24 hours	1490	.....	.....	11.72	.....	11.93	
Intake	1760	.....	.....	8.5	.....	13.4	
Balance	+270	.....	.....	-3.22	.....	+1.47	

*Impression.* Normal reaction to the nephritic test meal. Note the variations occurring in the fluid output and the specific gravity, which are in inverse ratio; the night urine, which is small in amount and shows a high specific gravity and a high percentage of nitrogen, and the approximately normal output of water, salt, and nitrogen.

Regulation of the diet is one of the most essential features of treatment. Thanks to our functional studies we can now base this upon the individual requirements of the case, not upon so-called general principles. The three factors to be considered are the fluid, the salt, and the nitrogen intakes. Practically all of these patients require limitation of their fluid intake, the degree of limitation depending upon the observed lag in water output and the amount of edema. It is scarcely possible, however, to discuss the water exchanges separately from the salt, since in these patients they are concurrent. The most distinctive result of the test meal in myocardial insufficiency, without renal involvement other than chronic passive congestion, is a low-water output with fairly high specific gravity, nearly always 1020, extremely low salt concentration and total output, and, in contrast, a normal nitrogen excretion brought about by the high concentration of this substance in the urine. The greater the degree of accompanying contraction of the kidney the more the specific gravity tends to be fixed and at a low level, nocturnal polyuria to become marked, and the concentration of the nitrogen, especially in the night urine, to fall far below the normal. With any of these features in evidence it is necessary to further test the functional capacity of the kidney for nitrogen by the determination of the blood urea and, best, by the comparison of this with the urinary urea in the Ambard formula. Whether this is better expressed, as in the recent admirable work of McLean, of the Rockefeller Institute, as an index of urinary

excretion, on the basis of a normal standard of reference of 100, or by Ambard's coefficient, the normal value for which is 0.06 to perhaps 0.09, is not clear to me. It is desirable that we should not have to burden our minds with any unnecessary arbitrary numerical values. Since Ambard's coefficient is already widely used the desirability of another set of values for expressing the same functional test should be clearly demonstrated before being adopted. The new values have mnemonic simplicity in that 100 is ideal perfection and the calculation is much simplified, but the range of normal values, from 80 to over 200, is rather wide.

A high Ambard or a falling index of urea excretion, or blood nitrogen above the normal, indicates the need for limitation of the protein intake. Ambard considers the normal constant 0.07. Unpublished observations by Lewis, in our clinic, show that 0.09 is more nearly the upper normal limit. There is considerable difference of opinion as to the figure for urea which may be found in the blood of healthy persons, but our experience coincides with McLean's<sup>10</sup> that 50 mgs. per 100 c.c. is possible with very high protein diet. Apart from this, 40 mgs. should never be exceeded. The urea nitrogen is practically one-half of this. The total non-protein nitrogen should rarely pass 40 mgs. per 100 c.c. under any circumstances. The small range found by Folin and Denis<sup>11</sup> in absolutely healthy individuals, 22 to 26 mgs., is too ideal a standard to apply to patients. The practical means for accomplishing this limitation vary from a low protein diet, which can never be an exclusive milk diet, to the introduction of short periods of nitrogen starvation in the worst cases. In such periods carbohydrate food should be given freely to spare protein. A satisfactory low-protein diet devised by Mosenthal for use in our wards follows:

#### THE JOHNS HOPKINS HOSPITAL.

##### LOW PROTEIN DIET.

###### Breakfast:

- Sherry, 30 c.c.
- Baked apple, stewed prunes, orange.
- "Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch).
- Cream, 15 c.c.

###### Dinner:

- Sherry, 30 c.c.
- Potato, baked or mashed.
- String beans, cabbage, carrots, lettuce, onions, tomatoes, cucumber pickles.
- Fruit cornstarch pudding, fruit tapioca pudding.

###### Supper:

- Same as dinner. (Salt, sugar and butter may be used as desired, and need not be weighed.)

<sup>10</sup> The Numerical Laws Governing the Rate of Excretion of Urea and Chlorides in Man, *Jour. Exp. Med.*, 1915, xxii, 212, No. 2; 1915, xxii, No. 3.

<sup>11</sup> Protein Metabolism from the Standpoint of Blood and Tissue Analysis—Sixth Paper, *Jour. Biol. Chem.*, 1913, xiv, No. 1.

## NITROGEN CONTENT OF FOODS USED IN LOW PROTEIN DIET.

Article of food.	Percentage of nitrogen.
Cream . . . . .	0.41
Cereal:	
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch) . . . . .	.13
Fruit:	
Baked apple . . . . .	.04
Orange . . . . .	.16
Stewed prunes . . . . .	.14
Vegetables:	
Cabbage . . . . .	.16
Carrots . . . . .	.10
Lettuce . . . . .	.24
Onions . . . . .	.17
Cucumber pickle . . . . .	.10
Baked potato . . . . .	.48
Mashed potato . . . . .	.40
String beans . . . . .	.23
Tomatoes . . . . .	.23
Desserts:	
Blackberry cornstarch pudding . . . . .	.05
Prune cornstarch pudding . . . . .	.07
Apple tapioca pudding . . . . .	.02
Peach tapioca pudding . . . . .	.06

Failure to eliminate salt makes essential the reduction of the salt intake to a figure below the twenty-four-hour output. Where much edema exists a rigorous salt-poor diet containing less than 3 grams, if possible getting the amount down to 1 gram, is most desirable at the start. Since these patients with myocardial insufficiency and marked edema require strict limitation of fluids as well the Karell diet is ideal. As is known, this consists of 800 c.c. of milk in the twenty-four hours as the only food or fluid allowed. Karell was a Russian physician who introduced this diet as a somewhat empirical cure for dropsy fifty years ago. We now possess entire theoretical justification for its use as a rational measure of safeguarding treatment, which is also highly effective in the cure of a most distressing symptom. It has the great virtue of simplicity. It can be carried out in households where an accurate salt-poor diet of any other kind would be impossible. Disappearance of edema usually begins after two or three days in this myocardial group of patients, and is little short of magical. When diuresis is abundant and the dropsy disappearing rapidly the amount of milk can be gradually increased up to 1500 c.c., and then other appropriate foods gradually added. It is desirable to determine the degree of restoration of the power of the kidney to excrete salt before allowing return to a full diet. All such patients should be warned against the abuse of salt for the future, and must never take large volumes of fluid or bulky meals. I think tobacco should be forbidden, but I am not sure that a little alcohol is harmful.



After recovery from the urgent symptoms the return to physical activity must be by very gradual stages and carefully supervised. Massage, resistance movements, and hydrotherapeutic procedures are all helpful here. Fibrillating cases must, if they show any tendency to a rate above the normal, take small doses of digitalis more or less constantly, the dosage to be determined by observation.

4. General edema without notable myocardial insufficiency the prominent symptom. This group of patients is much smaller than the preceding, and is met more frequently in hospital wards than in private practice. A considerable proportion of these dropsical patients have a subacute or chronic diffuse nephritis—that is a true inflammatory lesion of the kidney involving glomeruli, tubules, and interstitial tissue. This was what Dr. Delafield called chronic diffuse nephritis with exudation. Their urine is highly albuminous, and contains casts of all kinds. The common name given this type of disease, chronic parenchymatous nephritis, is altogether a misnomer. A number of them, under careful treatment, prove to be cases of very protracted acute nephritis, and will eventually make a functional recovery. Others develop increasing renal insufficiency with uremia and enter the next group, which I shall describe later. A few patients of this type, with the most obstinate edema and low blood-pressure, prove at autopsy to have amyloid kidneys. Still others are examples of a degenerative lesion of the tubular epithelium, not an inflammatory process. The cause of this we do not know, but its similarity to the effects of certain inorganic poisons makes a chronic intoxication plausible. The pregnancy kidney is a special example of this type. Following Friedrich Müller, Volhard and Fahr<sup>12</sup> in their recent book use the term nephrosis to describe these non-inflammatory cases. Their diagnostic criteria are the absence of blood elements in the urine and the absence of a rise in blood-pressure. Those who are interested in the pathology of renal disease I would refer to this admirable anatomical and clinical monograph. Widal,<sup>13</sup> on the other hand, adopts a purely functional classification. While I do not believe the functional disturbances permit of so clean-cut a subdivision of renal disease as he makes, and should be personally dissatisfied with a diagnosis which did not rest upon an anatomical basis, still this particular type has so predominant a disturbance of the salt and water excretion as to justify his name salt-retention nephritis. Certainly for treatment this is the essential feature to recognize, and Widal and Javal's<sup>14</sup> work on the effects of withholding and feeding salt in such cases has been one of the great recent advances in practical therapeutics. When tested, either by the nephritic

<sup>12</sup> Die Brightsche Nierenkrankheit, Berlin, Julius Springer, 1914.

<sup>13</sup> Les Grands Syndromes du Mal de Bright, Jour. med. français, Paris, 1911, v, 18-33.

<sup>14</sup> La cure de déchloruration, Paris, J. & B. Bailliére, 1906.

test meal or by the addition to a constant diet of an added ten grams of salt, these patients all show a striking failure to excrete sodium chloride. The salt concentration in the urine is often as low as 0.1 per cent., and the daily output not over one gram for long periods. With this the amount of urine is naturally very small and the retained water and salt accumulate in the subcutaneous tissues or serous sacs. Whether in all these cases the power of the kidney to excrete salt is primarily affected is very doubtful. It is highly probable that in many an increased affinity of the tissues for water, is equally important with the state of the kidney. For practical purposes of treatment it makes no difference. Salt and water are being retained. The 'phthalein test and the ability to excrete nitrogen may show unimpaired kidney function in every other respect. The potassium iodide test of Schlayer shows tremendous delay in excretion, but to me has no practical significance. The important point to determine is the degree of impairment of the ability to excrete water and salt. One patient may put out five grams of sodium chloride a day, another only one gram. For the first a diet containing three grams will lead to disappearance of the edema; for the other the most rigorous salt-poor diet will be without effect. Treatment should always begin by a period of very low salt and water intake to promote rapid absorption of the dropsical effusions. When this has been accomplished the response to increased water intake should first be tested and fluid pushed as fast as it can be excreted. The response to added salt should later be tested from time to time and the intake gradually increased, with care to keep always below the tolerated amount. Bed is desirable until normal function is restored. The problem of further treatment is that of the convalescence from acute nephritis. Local foci of infection should be looked for and the patient safeguarded from exposure, strain, and all injurious surroundings.

Patients with very low salt outputs and obstinate edema require accessory dehydrating measures, of which sweat baths have, in my experience, been the most effective. Purging may be of some value. In one patient hot packs were promptly followed by diuresis, the absorption of an obstinate edema of nineteen months' standing, and a prompt rise in the salt concentration of the urine. Retention with recurrence of edema was immediate upon cessation of the packs, and again disappeared upon their resumption. Such an influence is hard to explain, but suggests an alteration in the kidney circulation, acting upon the lesion itself. Borderline cases between this group and the preceding require a suitable combination of cardiac therapy with that just outlined.

5. Advanced renal insufficiency, uremic symptoms superimposed upon one of the foregoing types. We all recognize this as the classical picture of the end-stage of chronic Bright's disease. It is much easier to recognize than to define. Uremia can best be considered

with Ascoli as the varied disturbances, chiefly of the central nervous system, seen clinically in association with disease of the kidney or obstruction of the urinary tract and not dependent upon gross anatomical lesions of the brain. The differentiation of the severe headache of uremia and that due to cerebral vascular disease or of a uremic from an organic coma or hemiplegia may be very difficult. Lumbar puncture sometimes gives the clue, and should be resorted to. The gradually developing uremia which I have in mind here, however, with increasing headache, attacks of vomiting, respiratory disturbance, irritability, delirium, or drowsiness, gradually passing into terminal coma, scarcely permits of confusion, except with similar toxic states, as in the end-stages of liver disease. Changes in the optic nerve or retina are practically always present in true uremia, and the functional tests show what we may well consider as quantitative renal insufficiency. The test meal can be safely used only in the early stages, and then should frequently have its protein content reduced. It will show nocturnal polyuria, fixation of the specific gravity at a fairly constant, sometimes an absolutely constant, level, which is low in proportion to the severity of the renal insufficiency. It indicates inability of the kidney to excrete the normal constituents in anything but low concentration. The functional picture is constant in advanced contracted kidney, but may vary from week to week in diffuse nephritis. In our experience both nitrogen and NaCl concentrations have been equally reduced. Frothingham and Smillie<sup>15</sup> have found this also. This makes Widal's distinction between nitrogen-retention nephritis and salt-retention nephritis invalid. Sodium chloride excretion may be affected as an isolated functional disturbance, but nitrogen excretion seems only to be affected in quantitative renal insufficiency in company with all of the other functions except that of water excretion, which may remain intact. This NaCl retention does not necessarily lead to edema. The patients often have great thirst, considerable polyuria, and loss of weight, with dryness of the skin and tissues. This dry salt retention emphasized by the French school is of much theoretical interest. The 'phthalein test is of diagnostic, prognostic, and therapeutic importance. The excretion is diminished in proportion to the degree of renal insufficiency, and, as a rule, parallels closely the Ambard coefficient and the degree of increase of the non-protein nitrogen of the blood. When blood analyses are not possible it is the best practical measure of the probable degree of nitrogen retention, so-called. Agnew<sup>16</sup> has shown that in experimental renal lesions the blood nitrogen remains normal when the 'phthalein output is over 40 per cent. for the

<sup>15</sup> A Study of Different Nitrogenous Diets in Chronic Nephritis, *Arch. of Inter. Med.*, 1915, xv, 204.

<sup>16</sup> Comparative Study of Phenolsulphonephthalein Elimination and the Incoagulable Nitrogen of the Blood in Cardiorenal Diseases, *Arch. Int. Med.*, 1913, xiii, 485.

two hours. The most advanced cases excrete mere traces. All subsequent observers have confirmed the importance of Rowntree and Geraghty's<sup>17</sup> test in the prognosis and management of these cases.

The Ambard<sup>18</sup> coefficient is always raised and is unquestionably the most accurate measure of the degree of impairment of the urea excretion, though data in a large number of cases are not yet available. Widai's figures for blood urea remain the nearest approach to a prognostic standard if one remembers that they were obtained by the hypobromite method and represent more nearly total non-protein nitrogen. With 50 to 100 mgs. per 100 c.c. a long survival is possible, though prognosis must be guarded. With more than 100 mgs. no case lived over two years nor over one year if 200 mgs. were found. Over 500 mgs. were only found just before death. Certainly, in our experience, no case with over 300 mgs. of total non-protein nitrogen per 100 c.c. or an Ambard above 0.4 lived many weeks. On the other hand, Foster<sup>19</sup> has shown that low blood nitrogen does not insure a good prognosis.

Treatment of the severest renal insufficiency is purely symptomatic and not a cheerful duty. The distressing paroxysms of dyspnea and of Cheyne-Stokes breathing usually demand special relief. The low alveolar  $\text{CO}_2$  shows acidosis, but alkali has not relieved the symptom. For many patients morphin alone is effective, but it is a two-edged sword—it occasionally precipitates the rapid onset of anuria with coma, and once begun has to be used in increasing doses. Nothing requires more judgment on the part of the physician. Chloral hydrate in 5 or 10 grain doses, alone or combined with moderate doses of bromides, is sometimes very effective and should always be given a trial. Insomnia is commonly bound up with the onset of dyspnea on first lying down or with the recurrence of dyspneic paroxysms through the night. One serious practical mistake made by many physicians is to insist on these sufferers going to bed. Instead they should be encouraged to sleep in a chair until one is sure that he can promise them a real sleep in bed. Bed soon acquires for them a mental association with respiratory distress, and acts by suggestion as well as directly. The breaking up of this suggestion through a few good nights in a chair may make possible the return to restful sleep in bed. In some of the milder cases I have had great success by the use of a vasodilator just before retiring. For this purpose I prefer sodium nitrite, the effects of which are more lasting. It should be given about fifteen minutes before bedtime.

The gastro-intestinal disturbances, I believe, are of central nervous origin or eliminative. I feel sure that water and NaCl

<sup>17</sup> An Experimental and Clinical Study of the Functional Activity of the Kidney by Means of Phenolsulphonephthalein, *Jour. Phar. and Exp. Ther.*, 1910, i, 579.

<sup>18</sup> *Physiologie Normale et Pathologique des Reins*, 1914, Paris, F. Güttler.

<sup>19</sup> Functional Test of the Kidney in Uremia, *Arch. Int. Med.*, 1913, xii, 452.

are removed by vomiting and perhaps a little of the retained nitrogen. Treatment is apt to be very ineffectual. Lavage of the stomach and of the bowel are worth trying, but for the most part it is a problem in the use of general sedatives.

Diet is usually reduced to a minimum by the patient, for anorexia is the rule. In the severer degrees of insufficiency only starvation can hinder the nitrogen accumulation, and nothing prevents the terminal rise in blood nitrogen. In the early cases a very low nitrogen diet is strictly indicated with nitrogen starvation on days of severe symptoms, giving as much carbohydrate as possible. We have had a few remarkable improvements from this treatment. More frequently it is merely a choice of evils. The amount of fluid should depend upon the urinary output, and should be limited only by this or by the occurrence of edema. Vomiting, of course, will entail self-limitation. Of direct measures to reduce the retention of poisons, bleeding takes first place, but bleeding increases the anemia, which is so apt to be a feature of the intoxication. In a few recent cases repeated bleedings with consecutive transfusion have produced definite symptomatic improvement, and at times seemed to hold the blood nitrogen down. We have hoped that Abel's<sup>20</sup> operation of plasmapheresis might prove useful in these cases. It consists in bleeding into a non-clotting solution, separation of plasma and corpuscles by centrifugation, removal of the plasma, and reinjection of the corpuscles suspended in Locke's solution. One case done with hirudin, which was quite harmless to Abel's dogs, had a violent febrile reaction with shock, but recovered later and was considerably improved. We are cautiously testing the procedure further, using citrate, but have no successes to report as yet.

Bleeding has its greatest value in the case of sudden convulsive seizures. These so-called acute uremic or eclamptic convulsions have, in my experience, occurred in patients who did not have advanced renal insufficiency with marked nitrogen retention. The removal of at least 500 or 600 c.c. of blood is regularly indicated and recovery is common. I have known a number of such patients to live for several years after severe convulsions. I believe that the causation of these convulsions is analogous to that of the convulsions which occasionally mark the onset of acute scarlatinal nephritis, and has nothing in common with the causation of the chronic uremia which accompanies advanced renal insufficiency. Many are undoubtedly due to cerebral vascular disease. Sweating occasionally seems to benefit the patient.

The most important treatment in uremic cases is of associated myocardial insufficiency, when it exists. The superposition of chronic passive congestion on moderately damaged kidneys may

<sup>20</sup> Plasma Removal with Return of Corpuscles (Plasmapheresis), *Jour. Phar. and Exp. Ther.*, 1913, v, 625.

precipitate severe renal insufficiency. In other words a person who has lost the part of his reserve kidney tissue which constitutes the factor of safety, and is, roughly, about two-thirds of the total, may be thrown into the severest renal insufficiency by purely functional disturbance of the kidney circulation, as he may also be by the occurrence of an acute intoxication or infection leading to fresh anatomical lesions of an acute type. The prognosis when myocardial insufficiency is marked is always much better, because the element of functional disturbance may be recovered from under appropriate treatment of the heart, while gradually increasing renal insufficiency, due to progressive destruction of the kidney tissue, must have an absolutely hopeless outlook.

Of equal importance, but less generally appreciated, is the urgent necessity for the treatment of any associated obstruction of the urinary tract. Back pressure from an enlarged prostate with even moderate residual urine, combined with an only slightly damaged kidney, may rapidly lead to severe renal insufficiency, with uremia. The recent work of the genito-urinary surgeons in this field should be familiar to all medical men. The extent of the damage to function is demonstrated by the phenolsulphonephthalein test, as Rowntree and Geraghty<sup>21</sup> early showed in patients from Dr. Young's urological clinic, and Mosenthal has found the same indications in the study of such patients with his test meal. I have personally seen what was apparently advanced contracted kidney, with extreme hypertension and serious uremic symptoms, in a man, aged seventy-six years, transformed to a comparatively benign arteriosclerosis of the kidney, with hypertension, after the relief of back pressure by removal of the prostate. The patient was restored to practically ordinary health and working ability for a man of his years. In elderly men especially the possibility that urinary obstruction is the chief cause and renal disease the accessory cause for renal symptoms should never be out of mind. Pyelitis and pyelonephritis may produce similar pictures. Modern surgery in such conditions may make medical management superfluous.

A final word as to the possibility of surgical treatment in uncomplicated nephritis. Reginald Harrison first proposed this nineteen years ago, calling attention to the possibility of mechanical damage to the kidney circulation by pressure of the unyielding fibrous capsule upon a swollen edematous kidney. He proposed the relief of this mechanical factor by incision of the capsule. Five years afterward the late Dr. Edebohl, of New York, proposed to restore a damaged kidney circulation by decapsulation and the production of a collateral circulation between the cortex of the kidney and the surrounding tissues, and somewhat later Sippel advocated decap-

<sup>21</sup> The 'Phthalein Test: An Experimental and Clinical Study of Phenolsulphonephthalein in Relation to Renal Function in Health and Disease, Arch. Int. Med., 1912, ix, 284.

sulation of the kidney for puerperal eclampsia. The whole subject has been recently well reviewed by Ruge in the *Ergebnisse der Chirurgie und Orthopädie*.<sup>22</sup> He makes it clear, in spite of considerable contradiction in the interpretation of the results obtained, that we medical men should more carefully consider the possibility of improvement by nephrotomy or decapsulation in certain cases both of acute and chronic nephritis which do not respond satisfactorily to our usual measures. The need for better methods of treatment is plain. The field is peculiarly one for coöperative studies. I have personally witnessed a number of failures, but two cases stand out in my experience which I would record in this connection:

Both had persistent edema, hypertension, retinal lesions, and uremic symptoms extending over months, under my observation, in St. Luke's Hospital, New York. Both made an eventual complete functional recovery, being left only with albumin and casts in the urine and a moderate elevation of blood-pressure. Even the retinal lesions disappeared and both were well seven years later. Both had decapsulation performed. In one the improvement followed so closely as to suggest that the operation was its cause. The other had been decapsulated before she came to us, and improvement was so long delayed as to make the relation wholly improbable. I have seen no other recoveries after decapsulation in patients with severe renal insufficiency. I am inclined to believe that these two patients had a protracted subacute diffuse nephritis, and that the inflammatory process subsided without assignable cause, though possibly some remote focus of infection ceased to act as a portal of entry. In the first I feel sure, however, that the operation, probably by relieving tension within the capsule and improving the blood flow through the kidney, at least hastened the recovery. One would not anticipate any advantage from operation on advanced contracted kidneys.

In conclusion, may I emphasize the obvious summing up of the whole matter. Improved methods of investigation now permit of the much more accurate analysis of the various factors entering into the production of the complicated symptomatic pictures of chronic renal disease. Such analysis makes possible the more exact adjustment of treatment to the needs of the individual case and the relief of the patient from burdensome and unnecessary restrictions. In spite of all this it brings us not one whit nearer the real goal of treatment, prevention, or cure of the disease. If we ever achieve this it will be through new knowledge of the causes of these obscure but frequent affections, and every attempt to approach this problem from a new view-point should be enthusiastically welcomed by every medical man.

<sup>22</sup> Ueber den derseitigen Stand einiger Nephritisfragen und der Nephritischirurgie, loc. cit., 1913, vi, 565; see also Jour. Am. Med. Assn., October 2, 1915, lxx, 1188.

## THE RELATION OF PROGNOSTIC FACTORS TO TREATMENT IN DIABETES MELLITUS.

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WE are not in the habit of considering those factors which influence prognosis as intimately related to the problem of therapeutics. The reason we do not do so is because we customarily think in the terms of acute disease. The necessity of considering prognostic factors therapeutically is self-evident. When a man suffering from chronic renal disease is advised to seek a mild winter climate the physician is trying to avoid the danger to his patient from pneumonia. He considers a prognostic factor as a problem in preventive therapeutics. He may not ponder, but he knows that of individuals with chronic disease only a minority die of that disease, the majority, weakened and undermined in health, die of acute superimposed infections or of complications. The apt formula of a famous American physician on how to live to old age is pat: "Acquire a chronic disease and take care of yourself."

If, then, we are to advise intelligently patients with maladies such as chronic nephritis, and diabetes we must form a very clear estimate in each case as to just what the dangers are which menace his existence. This is necessary in order to carry out the prime endeavor of prolonging life—and it is no less requisite that we consider these factors in the means adopted to ameliorate the symptoms of the disease. The two goals of therapeutic endeavor, prolongation of life and the amelioration of symptoms, are secured but seldom by a change in the individual; not infrequently by a change in the environmental demand. Therapy directed to etiological factors is at present almost unknown in the realm of chronic disease.

These principles find no better example than in the treatment of patients with diabetes mellitus. With this disease, perhaps, more than with any other, the afflicted is out of joint with his environment; he can no longer eat or work with his brother man. We are apt not to think of it, but the condition is appalling. Every single human privilege is walled off by an adaptation to a narrowed function.

Now what are the dangers which beset the existence of the patient with diabetes? Numerically infections take first rank and account, directly or indirectly, by precipitating coma for over 78 per cent. of the deaths. Elsewhere<sup>1</sup> I have called attention to the frequency of surgical infections, but I do not wish at present to limit my

<sup>1</sup> Diabetes Mellitus, Philadelphia, 1915.



remarks to any one type. Even a slight cold becomes a very serious complication with a diabetic child; tonsillitis that would hardly confine a healthy man to the house has sent many diabetics to the grave. Tuberculosis is proverbially common among diabetics seen in hospital practice, less so among the well-to-do. Pneumonia, in my experience, has been invariably fatal, often because it precipitates acidosis and coma. Since these dangers which kill the majority of diabetics menace all alike, any mode of treatment which disregards these prognostic factors is lacking in foresight. Once contracted, infections are difficult in any case to combat, and often the fight is hopeless; the only safety is in keeping the patient in some condition approximating to normal vigor, so that infective agents find a less fertile soil. This principle concerning infections, as related to bodily vigor, is established, and finds no exception in the realm of chronic disease. Disregard of one ultimate aim of therapy in diabetes—namely, an approach toward a healthy state of resistance to infectious disease, so often leads to calamity that I am frankly pessimistic for that group of cases that can attain and preserve a sugar-free urine only at the expense of nutrition. With a sufficient number of cases it will, I think, be manifest that one danger has been exchanged for another.

There is no question in my opinion that the *average* diabetic not only has more comfort and sense of well-being when his urine contains no sugar, but that his actual resistance to infection is higher. I refer now to cases in middle life in which a severe glycosuria is not complicated by acidosis and in which undernutrition and loss of strength are the striking features. The majority of these cases regain strength and energy after the glycosuria is controlled. With others the diet which controls the glycosuria necessitates that the patient remain some 20 per cent. under normal weight, while with a diet that holds him but 10 per cent. under weight he has about fifteen grams of sugar daily in the urine. Now which is the preferable condition? Neunyn said that he did not know, and I doubt if we do at present. Again, exercise benefits the majority, but some patients have slight rises in temperature after exercise, and without the exercise the tolerance is too low for safety. It seems to me that here we have questions not related to our ideals of treatment but intimately concerned with the future of our patient, and they are best decided by remembering from what direction danger approaches.

As to whether a sugar-free urine indicates a state of affairs in the body economy which may be spoken of as holding the diabetic tendency in control, I have some doubts. There are facts which speak against it, as, for example, the frequency of pathological organic changes which develop after long periods during which the diabetes is apparently under full control. I refer to renal disease in the younger patients and nerve lesions in all. As a matter of fact,

we are not able to effect the end we strive for. As proof that we are not overtaxing the body's powers to handle sugar, we customarily accept the fact that the urine does not contain glucose. But this is not the criterion. The real criterion is the percentage of blood sugar; and with any cases other than the mild ones the blood sugar remains above normal and can be reduced to normal only during periods of excessively low diet or absolute fasting. In other words, there is a considerable margin between the maximal normal (0.14 per cent.) of blood sugar concentration and the *threshold of renal permeability* (0.16 to 0.17 per cent.); constant hyperglycemia means a continuation of an abnormal state. We can successfully remove the overload, it is true, when we reduce the blood sugar from 0.35 or 0.45 per cent. down to 0.16 or 0.17 per cent., and with the majority of patients that reduction effects a wonderful change in general health. But 0.16 per cent. is not a normal blood sugar. The blood then and not the urine is the measure of whether the means we employ are suitable. With some of the severest and most hopeless cases that have come under my observation the urine contained no sugar at a time when the blood sugar, due to a concomitant kidney disease, was as much as three times the normal. Evidently the urine may mean nothing as to the diabetic state.

To excessive hyperglycemia is in my opinion to be assigned a large degree of impairment of function, and this idea I can best make clear by an analogy drawn from chronic nephritis. It is a common observation that with these cases of chronic renal disease at periods before treatment, all the tests and the metabolism studies may indicate a hopeless degree of renal damage, the urea of the blood may be very high and the 'phthalein excretion reduced to traces. After an appropriate regimen the same tests indicate a clear-cut increase in the ability of the kidney to perform its function. This phenomenon we may style a depression of function due to the overload. With diabetes the state of affairs is not very different. At times when there is marked hyperglycemia the tolerance appears *nil*; after a couple of months of treatment, when the blood sugar is reduced to only a little over normal, there is often a surprising ability to use carbohydrate. For this reason I think it is impossible to tell in advance whether any given case is mild or severe. Many that seem severe in the beginning, even with considerable acidosis, prove after a year to be only mild. But this is true *only when* the disease is *not of long duration*. With cases in which the indications are that a year or two at most have passed before treatment is commenced, my results have been very encouraging when the patients could do what their disease demanded. For this reason I shall divide my cases into two groups, early and advanced. The severity of the acidosis or glycosuria with these cases in the beginning was no criterion of the actual conditions, and this is adequately demonstrated by cases that were infused at the commencement

of treatment because of incipient coma. The history with these cases indicated about a year's duration of the diabetes. Some of these individuals are now using, on five days of the week, unrestricted amounts of starch without resultant glycosuria. One of them has a normal blood sugar unless the routine vegetable day be omitted for several weeks. All are young, under thirty-five years, and all are up to normal weight and vigor. These and other cases I have studied illustrate the difficulty stated by Joslin in differentiating mild from severe diabetes. I know an old gentleman who was a severe diabetic at the age of twenty-two years. He is now nearly seventy and has had no glycosuria for forty years. He was a patient of the elder Shattuck. In fact, I question whether the terms mean just what we wish to express when we speak of young patients with glycosuria and severe acidosis. Should we not rather say early and advanced? (The older cases are in a class by themselves in which acidosis is but seldom of moment, even when of considerable degree, as Neunyn pointed out.) My experience of the last five years has been that with young adults who came under observation early after the disease was recognized, all have secured sugar-free urines, notwithstanding severe acidosis at the start, and all who followed advice have recovered a considerable degree of tolerance for carbohydrate, much above what it was in the beginning of treatment.

Concerning the cases of young adults, four to five years of age, who were observed first when the disease was of some years' duration—that is, advanced cases—the results have not been encouraging even when, as often happened, on account of but slight acidosis, it appeared in the beginning that the task was much easier than with some of the early cases. The glycosuria may be easily controlled, but the blood sugar is difficult to reduce to normal, and it remains normal only under the most restricted conditions. As a rule, the tolerance secured is too meager to preserve health over long periods. My observation indicates that with this group those patients who have adhered to diet have died of complications and infections wherein coma occurred only as a sequel to acute disease, *i. e.*, pneumonia or la grippe. Of those who have not been so rigidly dieted or who have not observed diet with due care the majority have died in coma. The period of life in both groups averages over two years from the beginning of treatment. An estimate of value of treatment as measured in years of life can be discovered only by a very large number of cases observed for years. The point is that with advanced cases in young persons the results are discouraging even when the disease is apparently under control. And I might add here that this statement applies also to diabetic children. Cases now living that have been for several years ideal so far as absence of glycosuria indicates, are under height, under nourished, and altogether most pathetic.

One interpretation of these facts as I understand them is this: That with *early* cases we can expect much from treatment. Vigilant control of the diet so that glycosuria is absent and the blood sugar down to nearly normal is justified, since with time tolerance increases. Even a dangerous degree of acidosis does not necessarily frustrate this design. This interpretation rests on the hypothesis that I have stated earlier in the paper—namely, that the hyperglycemia itself induces pathological function. The alternative interpretation is that these early cases that are now doing well will eventually deteriorate and become the typical advanced case. It will take years to decide this point, but against this contention is the increased tolerance for carbohydrates observed as years go by. It is to be remembered, however, that some young adults with severe diabetes and considerable acidosis live six to ten years under the less stringent methods which aim only to keep sugar excretion low, but never abolish it completely. But it is my belief that with those cases in which the diagnosis is made early much can be accomplished by vigorous treatment. It matters not whether the blood sugar be reduced by the rapid method of complete fasting or by the slower method of periodic fasts; *the end that must be attained is a sugar-free urine, blood sugar as near normal as possible, and an absence of acidosis.*

The chief danger lies in the after period, when because the urine is so persistently normal, patients, and even physicians, are led to doubt the necessity of the diet, with consequences that are sometimes serious. With young patients, early or advanced, the danger to be feared is acidosis, and our therapeutic endeavors are directed to prevent its development or abolish it after development. When there is no acidosis I have never been compelled to resort to fast days as a means of controlling the most extreme glycosuria, although there is no doubt the end can be attained most rapidly by the complete withdrawal of food. The question is, then, is starvation always safe? It has been generally believed, and was emphatically stated by Neumyn, that an acidosis tendency once established is prone to recur. With diabetics as with normal persons, starvation induces acidosis, and even this, I think, can and should be avoided, since one can not tell where it may lead. Cases that I have seen in consultation have made me more definite in this impression. In two recent instances an alarming acidosis, initiated by fasting, necessitated heroic measures which availed to save the life of only one patient. These unfortunate issues we are not at present able to prevent unless the patient be in a hospital, and adequate warning of danger be watched for in the laboratory studies.

Turning now to cases in which acidosis dominates the picture and in which the disease is of long duration, the therapeutic problem is again different. The menace here is coma, and the fact that any of the patients can be relieved of their danger, even for a brief time

by fasting, is a *remarkable* contribution to our knowledge of diabetes. With cases that are in imminent danger of coma, in which each day may be the last, a measure that promises *any success at all* is of the greatest value; and here, I believe, is the special field for the fasting method. That fasting in itself may be a dangerous procedure, we recognize; as are also serious surgical measures. There are occasions when we have scant choice. That the fasting treatment is not devoid of hazard we must recognize, and it throws upon us the responsibility to use this method only when other and less drastic methods are inadequate to effect the desired result; and to recognize that fasting is, again, like many surgical measures, suited best for use in well-equipped hospitals, in which careful observation and frequent tests of blood, urine, and alveolar air are made as part of the routine. Only in this way can dangerous reactions be foreseen and requisite measures be instituted. The treatment is *fundamentally* a treatment for grave acidosis.

Finally, then, I can summarize my conclusions: Every case of diabetes demands the most careful study not only of the diabetic state, but also of all conditions which may influence the future health of the patient. Infections must be kept in mind as the constant danger. Early cases must be kept free of glycosuria in order to raise resistance and to avoid the development of acidosis. This can be done even in face of acidosis by the use of restricted low diets. With advanced cases glycosuria must be controlled in order to regain normal weight and vigor. When there is grave acidosis this also can now with many cases be successfully abolished. The chief difficulty in treating all diabetics is the necessity of constant vigilance over years.

## THE EFFECT OF EXERCISE UPON THE CARBOHYDRATE TOLERANCE IN DIABETES.

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It has been known for many years that exercise increases the carbohydrate tolerance in the milder forms of diabetes, although in severe types of the disease it lowers the tolerance or may even precipitate coma. This therapeutic measure has been neglected, probably, because of the lack of a practical system of exercise the effects of which on patients could be checked up by an accurate test of the heart's functional capacity.

Our experience in treating patients with cardiac insufficiency by means of graduated exercise controlled by such a test, which we have described elsewhere,<sup>1</sup> suggested an experiment with these exercises on a few selected cases of diabetes.

The apparatus used consisted of dumb-bells weighing from 10 to 40 pounds each, and steel bars varying between 25 and 80 pounds in weight, with which different series of movements were carried out. The exercises were of a concentrated form, and were given an hour daily, three days in the week, generally in the late afternoon. Each series of movements lasted from thirty to one hundred and twenty seconds, and six to eight were given at each exercise period, so that the actual working time varied between four and sixteen minutes for the hour.

The first patient was a professional man, aged forty-two years, suffering from a mild form of diabetes. In November, 1909, an insurance company had discovered sugar in the urine. His tolerance at that time was 360 grams of white bread in twenty-four hours. His urine was kept practically sugar-free for the next four years. In June, 1913, his tolerance had decreased to 150 to 180 grams of white bread in the twenty-four hours. He was then put on one egg and vegetable day weekly. In October, 1913, his tolerance was still 150 grams, but by September, 1914, it had decreased to 120 grams.

On September 24, 1914, when the exercise course was started, the patient's physical examination was negative; he weighed 141 pounds and his lung capacity was 284 cubic inches.

The following table summarizes the results in this patient:

Date.	Quantity of carbohy- drate (white bread) in twenty-four hours (grams).	Quantity of glu- cose in twenty- four hours' urine.	Approximate amount of work at each period in foot- pounds.
September 23, 1914 . . .	120	trace	14,900
October 19, 1914 . . .	150	none	
November 2, 1914 . . .	180	trace	21,700
November 9, 1914 . . .	180	none	
November 16, 1914 . . .	210	trace	
November 23, 1914 . . .	225	none	
November 30, 1914 . . .	210	3.1 grams	36,500
December 14, 1914 . . .	225	none	
February 1, 1915 . . .	240	none	40,000
March 17, 1915 . . .	270	trace	
April 24, 1915 . . .	270	trace	
May 12, 1915 . . .	270	trace	

During the period noted above the patient's daily allowance of carbohydrate was always kept well below his tolerance. An egg and vegetable day was given once weekly. His tolerance increased from less than 120 grams on September 23, 1914, to 240 grams on February 1, 1915. Although his exercises were continued until June 1, 1915, we never could get his capacity much beyond that

<sup>1</sup> Barringer and Teschner, *Arch. Int. Med.*, 1915, xvi, p. 795.

figure. He gained six and one-fourth pounds in weight and his lung capacity increased from 284 cubic inches to 300 cubic inches. His general health and ability to do his work without fatigue improved markedly.

These results are truly astonishing when we consider that the actual working time of our patient during his course of fifty exercise periods amounted to between four and sixteen hours.

July 1, 1915, he stopped the exercises and in their stead lead an active outdoor life in the country for ten weeks. His exercise there was carried out quite systematically, and consisted chiefly in chopping down trees, chopping wood, and using a pick on a clam-shell road. He continued his weekly egg and vegetable day and kept his daily intake of carbohydrate well within his tolerance. To our surprise the tolerance decreased steadily, as is seen by the following table:

Date.	Quantity of carbohydrate (white bread) in twenty-four hours. (grams).	Quantity of glucose in twenty-four hour-specimen.
August 3, 1915	225	trace
August 13, 1915	195	trace
August 31, 1915	165	trace
September 20, 1915	120	none
October 5, 1915	150	none
November 21, 1915	180	trace
December 5, 1915	180	trace
December 19, 1915	195	trace
January 2, 1916	195	trace

On September 20 the patient returned to the city and resumed his dumb-bell and bar exercises. Through a misunderstanding he did them each day before breakfast, but on December 5 this was remedied. Also for three weeks they were omitted on account of an attack of lumbago. He now seems (December 19) to be approaching his former tolerance of 240 grams.

The second case selected was one of moderate severity. The patient was a professional man, aged thirty years, in whom a glycosuria had been discovered in 1912. Since then, in spite of following quite conscientiously a treatment initiated by Dr. von Noorden, his urine never has been sugar-free.

The following table summarizes our results:

Date.	Diet.	Glucose in twenty-four hour-specimen.	Exercise.
February 28, 1915	6 days carbohydrate-free	7.9 gms. (acetone +)	
March 16, 1915	60 gms. white bread	14.4 gms. (acetone 0)	
April 1, 1915	30 gms. white bread 150 gms. oatmeal	6.4 gms.	Three hours weekly, began March 20.
April 17, 1915	30 gms. white bread 150 gms. oatmeal	4.6 gms.	
May 1, 1915	30 gms. white bread 150 gms. oatmeal	10.2 gms.	
May 7, 1915	Egg and vegetable day	6.3 gms.	

This patient's weight increased from 135 $\frac{1}{4}$  pounds to 140 $\frac{1}{2}$  pounds, but the glycosuria was not at all influenced. His general health and ability to work were markedly improved.

The third patient was a business man, aged sixty-four years, who had had a mild diabetes for about five years, his tolerance being 60 grams of white bread in twenty-four hours. This was increased to 90 grams of bread after an extended course of exercises.

### **SOME ASPECTS OF THE CLINICAL STUDY OF THE RESPIRATION: THE SIGNIFICANCE OF ALVEOLAR AIR ANALYSES.<sup>1</sup>**

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ONE of the most striking developments in clinical medicine during the last decade has been the gradual substitution of the physiological for the anatomical point of view. Up to within a comparatively few years the chief basis of medicine was pathological morphology, and the chief aim of diagnosis was to determine the anatomical changes in the diseased organs. Recent advances in physiology and in biological chemistry, however, have exerted a profound influence on the attitude of the clinician, and have impressed on him the importance of approaching his subject from a much broader aspect. The problem of diagnosis is now not so much to discover what a given organ may look like, but what it is doing or what it is able to do. Pathological physiology is becoming more and more an object of investigation, and such terms as "functional tests" and "functional diagnosis" are already current in medical phraseology.

The application of the methods of physiology has already produced an abundant harvest of results in several fields. The study of polygraphic tracings and of electrocardiograms, both in man and in experimentally produced conditions in animals, has quite altered our conceptions of heart disease. New clinical conditions have been differentiated, and processes long recognized have been explained. In renal diseases the "functional studies" have thrown new light on the various types of nephritis, their course, prognosis, and treatment. Some progress has been made in the investigation of hepatic function in disease, but as yet, unfortunately, little of great clinical significance has been brought out. On the subject

<sup>1</sup> Read before the Springfield Academy of Medicine, March 9, 1915.



of respiration a large amount of important work has already been done. The greater part of this has had to do directly with the study of metabolism, of oxygen intake, and carbon dioxide output and their relation to heat production under various conditions. Until comparatively recently very little attention has been paid to the abnormalities of respiration itself, but the development of a more comprehensive knowledge of the physiology of respiration and the adaptation of new physiological and chemical methods have opened up fresh paths to clinical investigation.

From the point of view of clinical medicine some of the most significant of the recent investigations on the physiology of the respiration have been those dealing with the determination of the normal stimulus to respiration. Among the older physiologists one school held that the respiratory centre was stimulated by a lack of oxygen, while their opponents claimed that it responded to an excess of carbon dioxide in the blood. The work of Haldane and Priestley,<sup>2</sup> in 1905, settled the problem for the time being and seemed to prove conclusively that carbon dioxide is the effective stimulus to respiration. Their experiments showed that the respiratory centre is extremely sensitive to changes in the tension of the carbon dioxide in the blood. A rise of 0.2 per cent. in the carbon dioxide of the alveolar air was sufficient to double the pulmonary ventilation, while a fall below the normal resulted in the production of apnea. Subsequent work, especially that of Winterstein<sup>3</sup> and of Hasselbalch<sup>4</sup> showed that the action of carbon dioxide as a stimulus to respiration is not specific, but that it depends on the fact that carbon dioxide is an acid. Any other acid can replace carbon dioxide wholly or in part as the stimulus. Indeed, it has been definitely demonstrated that the respiration depends on the reaction of the blood, or, as it is technically called, on the hydrogen-ion concentration of the blood. Under normal conditions the reaction of the blood is very slightly on the alkaline side of the neutral point. Any tendency toward an increase in the acidity, whether it be caused by an accumulation of carbon dioxide, or of any other acid, acts as a stimulus to the respiratory centre and increases the ventilation of the lungs. Even the increase of respiration, which is caused by an insufficient supply of oxygen reaching the tissues, may be explained by this same mechanism, for one of the results of imperfect oxidation is the incomplete combustion of acid products of metabolism, and these intermediary metabolites, insofar as they are acids, may form a part of the respiratory stimulus.

Since, then, the chemical control of the respiration depends on the reaction of the blood, it will be readily seen that in order to understand the pathological changes in respiration one must bear

<sup>2</sup> Jour. of Physiol., 1905, xxxii, 225.

<sup>3</sup> Arch. f. die ges. Physiol., 1911, cxxxviii, 167.

<sup>4</sup> Biochem. Ztschr., 1912, xlv, 403.

in mind the conditions which regulate the reaction of blood. Henderson<sup>5</sup> has said that the normal reaction of blood is, like the normal body temperature, one of the important physiological constants. All modern work bears this out. The chemical processes within the body, and especially all enzyme reactions, proceed most advantageously at an optimum hydrogen-ion concentration, and for many the range of reaction through which they can function is a narrow one. Life itself depends on the maintenance of the reaction of blood and tissues within very small normal limits. Undoubtedly the fundamental problem is that of the maintenance of the normal reaction within the tissue cells, for in all probability most of the important chemical processes by which metabolism is carried on are intracellular, or at least are the result of the actions of substances formed within the cells, whose very formation and elimination into the blood depends on the balance of acid and alkali within the cell. At the present time there are no very refined methods of studying tissue reaction, though, as will be shown later, the so-called "alkali-tolerance" test seems to give a more or less rough index of any continued overproduction of acid in the body and of consequent exhaustion of the reserve alkali of the tissues. Until methods have been evolved which will lead us into the obscure field of cellular and of tissue metabolism we must be content with studies of the blood. The composition of the blood certainly depends in large part on the activities of the fixed cells of the tissues, and the newer investigations of the chemistry of the blood and of the intermediary products of metabolism which it contains are leading to a much more intimate knowledge of the chemical processes of the body than could ever be obtained by examinations of the excretions alone. In the maintenance of the normality of the tissue reaction the blood plays an important part. It carries bases to the tissues to replace those used in neutralizing acids, and it forms the medium by which the acid products of cellular activity are removed from the cell. Fortunately, however, in spite of the fact that carbon dioxide and other acid products of metabolism are continually passing into the blood, the organism is peculiarly well provided with means to preserve its normality. That the reaction of the blood is not affected by this addition of acids depends (1) on its chemical composition, and (2) on the means at its disposal for the rapid excretion of acids.

The chemical composition of blood is such that it is ideally adapted for the preservation of a constant reaction. It contains large amounts of weak acids and their salts—carbon dioxide and sodium bicarbonate, monosodium phosphate and disodium phosphate—and a high percentage of proteids which have both basic and acid characteristics. To solutions which are made up of such

<sup>5</sup> Science, 1913, N. S., xxxvii, 389.

combinations it is possible to add considerable quantities of acid without producing any marked change in the hydrogen-ion concentration. If, for instance, acid be poured into a solution consisting of monosodium and disodium phosphates, the balance between the two will be disturbed—there will be more of the monosodium phosphate and less of the disodium phosphate—but within rather wide limits there will be only a minimal alteration in the true reaction of the solution. Indeed, Henderson has shown that the balance of weak acids and salts in blood is such as to allow of the addition of the maximum amount of acid with the minimum alteration in reaction.

The constancy of the reaction of blood is furthermore upheld by the means which the body has at its command for the excretion of acid. Non-volatile acids are excreted by the kidneys. Henderson<sup>6</sup> has drawn particular attention to the remarkable efficiency of the kidneys for their task. By some specific mechanism they are able to separate acid from bases, secrete an acid urine from an alkaline blood, and retain base in the body for the further neutralization of more acid. Volatile acids, and chiefly, of course, carbon dioxide, are excreted in the lungs. In the pulmonary capillaries carbon dioxide passes out of the blood into the air of the alveoli until the carbon dioxide tension in the blood equals that in the alveolar air. Thus the tension of the carbon dioxide in the alveolar air corresponds to that of the blood, and, as will be seen, it is an index of acidosis. In their function of excreting acid the kidneys may perhaps be regarded as the fundamental regulators of the reaction of the blood, but as the lungs are much more sensitive they can maintain extremely delicately the constancy of reaction by their control over the volatile acids.

Any rise in the acidity of the blood stimulates the lungs to increased ventilation. With moderate exercise there is an increased production of carbon dioxide in the tissues. If this is sufficient to affect the arterial blood to the respiratory centre, the pulmonary ventilation rises and more carbon dioxide is excreted. The same happens when air is rebreathed from a closed space. The carbon dioxide in the inspired air, and consequently in the alveoli, rises. This causes a rise of carbon dioxide tension in the blood and an increased ventilation of the lungs. During severe exercises, lactic acid is produced more quickly than it is excreted by the kidneys, and Ryffel<sup>7</sup> has shown that it is increased in the blood.

Under such circumstances the lactic acid acts as a stimulus to respiration by increasing the acidity of the blood. The lungs respond, but in order to keep the hydrogen-ion concentration of the blood at its normal level there must be a reduction of the

<sup>6</sup> Jour. Biol. Chem., 1911, ix, 403.

<sup>7</sup> Jour. Physiol., Proc. Physiol. Soc., 1910, xxxix.

carbon dioxide below its normal. Thus associated with the rise in non-volatile acids there is a compensatory decrease in the carbon dioxide tension of the blood, and since the two correspond, in the carbon dioxide tension of the alveolar air. These conditions are indicated diagrammatically in Figs. 1 and 2.

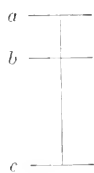


FIG. 1

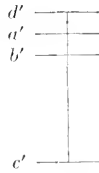


FIG. 2

In Fig. 1 the line  $a-c$  represents the acidity of normal blood;  $b-c$  is acidity due to non-volatile acids, and  $a-b$  is the acidity due to carbon dioxide.

Fig. 2 represents the conditions in acidosis due to a rise in the non-volatile acids, such as lactic acid in hard exercise or  $\beta$ -oxybutyric acid in diabetes,  $b'-c'$ , which is longer than  $b-c$  in Fig. 1, represents the increased acidity due to non-volatile acids. If the carbon dioxide remained unchanged, the acidity of the blood would be represented by the line  $d'-c'$ , an increase in the acidity of the blood which the organism could not withstand. In order to keep the acidity of the blood at its normal value,  $a'-c'$ , the rise in non-volatile acids is compensated for by a fall in carbon dioxide, so that the amount of carbon dioxide or, more accurately, the carbon dioxide tension, is reduced to  $a'-b'$ . Thus in conditions of acidosis the tension of the carbon dioxide in the blood or, what is the same thing, the tension of carbon dioxide in the alveolar air, gives an accurate index of the amount of the increase of non-volatile acid.

The demonstration that one of the chief functions of the respiration is to preserve the normal reaction of the blood, and that any increase in the acidity of blood acts as a stimulus to respiration, is of great importance in the consideration of pathological changes in the respiration. In the study of acidosis—of the increase of normal acids or the presence of abnormal acids in the blood—we possess a means of acquiring information concerning the stimulus to respiration and its variations in abnormal conditions. There are several general methods of approach by which one may find out about the formation of acids in the body. The examination of the urine with reference to its acidity, and to the presence of abnormal acids, while of a certain value, only tells about the acid which is leaving the body and does not necessarily give an accurate picture of conditions within the body. Of much more significance are studies of the blood itself. As has already been stated, the true reaction of the blood varies extremely slightly during life. Only in terminal

conditions has any marked deviation from the normal been found. Thus in most clinical conditions one does not expect that an increase in the formation of acids in the body will cause any actual change in the reaction of the blood, but merely a shift in the usual balance between volatile and non-volatile acids. In the pathological conditions associated with acidosis there is usually an increase in non-volatile acids and a consequent fall in carbon dioxide. The evidence of the presence of such a state may be obtained from the study of the blood or of the alveolar air, for the carbon dioxide tension of the alveolar air is the same as that of the blood.

The determination of the hydrogen-ion concentration of the blood is a complicated procedure. On account of its color, the high percentage of protein, and the influence of the carbon dioxide the simple colorimetric methods which may be used in urine are not practicable. The direct determination can only be carried out by means of electrochemical methods, and the difficulties of the technic are considerably enhanced by the importance of measuring the blood at a known carbon dioxide tension.<sup>8</sup> Barcroft<sup>9</sup> has devised a method by which the acidity of the blood is determined from the affinity which the hemoglobin shows for combining with oxygen under standard conditions. Both of these methods involve a highly specialized technic, but fortunately a very valuable index of the conditions in the blood may be obtained quite simply by means of an analysis of the alveolar air.

Under normal conditions, at rest, the carbon dioxide tension of the alveolar air is fairly constant. It shows only slight variations in different individuals, and in the same individuals at different times of day. The normal diurnal variations depend chiefly on diet. Thus on a pure carbohydrate diet the carbon dioxide extension is at a high level, while on a diet consisting largely of proteid or during starvation the tension tends to be lower. The normal variations, however, involve only a few millimeters and do not detract from the value of the determination in pathological conditions.

Samples of alveolar air may be obtained by several methods:<sup>10</sup> The first to be introduced was that of Haldane. In this method the subject gives a long, deep expiration into a piece of rubber tubing about four feet long. At the end of the expiration the entrance of the tubing is closed by the subject's tongue or by some form of valve, so that the expiration is held in the tube. By means of a small side tap near the mouth-piece, 25 to 50 c.c. of the air which constitutes the last portion of the expiration are withdrawn into a mercury filled gas pipette and subsequently analyzed. The last

<sup>8</sup> Arch. Int. Med., 1914, xiv, 236.

<sup>9</sup> The Respiratory Function of the Blood, 1914, Camb. Univ. Press.

<sup>10</sup> Arch. Int. Med., 1914, xiii, 497.

part of the expiration, particularly if the expiration is at least 600 c.c. deep, comes from the alveoli of the lungs, and if the expiration is sufficiently rapid its composition remains practically unchanged in its passage outward. In the hands of trained persons this method gives reliable results, and the figures obtained for carbon dioxide tension probably agree very closely with that of the arterial blood. Even with untrained subjects it is frequently possible to get satisfactory samples, but as it is necessary to have a very deep and rather rapid expiration there are many times when the method is unreliable. This is especially apt to be the case with persons of low intelligence or with patients who are sick and unable or unwilling to give a complete expiration. In such instances the method of Plesch as modified by Higgins<sup>11</sup> gives excellent results. A large series of observations made during the last two years at the Peter Bent Brigham Hospital with this method has demonstrated its simplicity and reliability in a considerable variety of clinical conditions. The method is based on the principle that if the subject breathes into and out from a closed space of suitable size for a definite period of time the diffusion of gases will be such that the composition of the air in the closed space will be similar to that in the lungs. In practice the nose is closed with a clip and the patient breathes through a mouth-piece, which is connected with a three-way valve leading to the outside air or into a rubber bag. The subject begins by breathing the outside air. At the end of an expiration the valve is turned so that the subject is connected with the rubber bag which contains about 1 liter of air. He takes four or five rather deep and slow respirations from the bag in twenty or twenty-five seconds. At the end of the last expiration the valve is again turned and the subject connected with the outside air. The bag, which is closed off by the same maneuver, contains air which is of the same composition as the air in the alveoli. Samples are then taken from the bag for analysis. The figures obtained for carbon dioxide tension by this method are somewhat higher than those obtained by the Haldane method, and they probably represent more nearly the tension of the carbon dioxide in the venous blood than in the arterial blood. In physiological studies the difference would be important, but in most clinical work the Plesch method gives results that fulfil all the necessary requirements. There are two chief sources of error in the method: The figures for carbon dioxide tension are too low if the respirations are very rapid and shallow, so that proper diffusion of gases does not take place. The results are too high if the subject is permitted to breathe from the bag for a period which exceeds in length one complete cycle of the circulation or approximately forty seconds. In general, however, constant and reliable results are obtained with little

experience. Three observations are usually made, and the analysis of the samples should agree within 2 mm. carbon dioxide tension. Occasionally one of the three varies so far from the mean that it has to be discarded. The analysis of air for carbon dioxide is extremely simple. By means of the Haldane gas analysis apparatus it can readily be completed in about four minutes. The figures for the normal tension of carbon dioxide in the alveolar air vary from about 38 to 41 mm. by the Haldane method and from 40 to 45 mm. by the Plesch method.

RESULTS OF THE STUDY OF PATHOLOGICAL CONDITIONS.

DIABETES. One of the first diseases in which it was recognized that acidosis played an important part and the disease in which the effect of acidosis on the respiration is most definitely manifested is *diabetes*. Probably on account of the incomplete or imperfect combustion of fats in severe cases of diabetes there may accumulate in the organism large amounts of  $\beta$ -oxybutyric acid, aceto-acetic acid, and acetone—substances which under normal conditions would be completely burned to water and carbon dioxide. This abnormal production of acids may go on for a long time without giving rise to any clinical symptoms, but when it reaches an extreme grade it becomes the most prominent feature in the case and eventually brings on the well-known clinical picture of "air hunger" and coma. During the early stage, while the production of acids is not excessive, the bases in the tissues and in the blood are sufficient to neutralize them, and their excretion is accomplished by the kidneys. At this period the ordinary mechanisms of the body are amply able to cope with the acidosis, so that there is no tendency for the reaction of the blood to be disturbed. If the condition continues, however, and the amount of acid increases, the reserve supply of base in the tissues will become exhausted in the attempt to neutralize the acid. The blood itself will be able to take up a considerable amount of acid without any effect on its true reaction, but beyond a certain point the addition of more acid will tend to cause a shift in the reaction of the blood. This increase in acidity will act as a stimulus to respiration and the normal reaction of the blood will be maintained by an increased pulmonary ventilation and a lowering of the carbon dioxide tension of the blood. The balance in the blood will be disturbed and there will be an increase in non-volatile acids with a corresponding drop in the tension of the carbon dioxide in the blood and in the alveolar air. This is the beginning of serious acidosis. The reserve supply of base in the tissues has been used up, the regulatory mechanism in the blood has begun to break down, and the organism is calling on its last reserves. If the condition progresses there will be a steady fall in the carbon dioxide tension of the blood until the symptoms of poisoning assert themselves. Finally the production of acids becomes so great that even kidneys and lungs together are unable

to excrete enough acid to keep the reaction of the blood within its normal bounds. The increased acidity of the blood stimulates the respiratory centre to greater efforts, and there results the enormous ventilation marked by the deep, rapid breathing which is so well termed "air hunger." Unless the formation of acids is reduced or their neutralization is brought about by some means, death from acidosis will ensue.

There are several methods by which it is customary to follow the course of acidosis in diabetes. Since these are usually tests applied to the urine they give evidence only of the amount of acid which is being excreted from the body. They give extremely unreliable information as to the amount of acid which is being formed in the body and as to the amount which is accumulating in the body. These latter are, after all, the factors of importance. What one wants to know is not how much acid the organism is getting rid of, but how much it is retaining, for it is the retained acid that is the source of danger. The commonest tests applied in diabetic acidosis are the qualitative tests for acetone and aceto-acetic acid. The attempt is usually made to get a general idea of the amount of each acid excreted from the degree of the reaction. The value of these tests is limited both by the fact that they give no conception as to the excretion of  $\beta$ -oxybutyric acid and because the information they do give may throw so little or such false light on the actual conditions within the body that an implicit reliance on them becomes extremely dangerous. In severe acidosis, and even in diabetic coma, the ferric chloride reaction is sometimes very weak. After the administration of alkali the reaction frequently becomes much more intense. On the one hand the patient may have been in grave danger from acidosis at the time when the urine showed evidence of a very small aceto-acetic acid excretion, while, on the other hand, the increase of the excretion of aceto-acetic acid may have been accompanied by a return to conditions within the body which are comparatively normal. Not infrequently one hears of cases of diabetes that went suddenly into coma without any previous warning. These are probably instances in which there has been an accumulation of acid in the body without any very marked excretion in the urine, so that even careful urine examinations have failed to call attention to the impending danger. It seems probable that the ammonia excretion is the best index which can be obtained from the urine, but even this will fail to give a correct quantitative picture in certain instances. As Poulton<sup>12</sup> has pointed out the ammonia in the urine depends (1) on its production in the body, and (2) on its excretion by the kidneys, and if either of these functions is disturbed the values obtained will fail to give a true estimate of the acidosis. It is, moreover, the total



amount of ammonia excreted in twenty-four hours that is of importance, and in many cases it is impossible to obtain complete collections of urine. Even at best the method does not allow one to obtain the immediate information that is so often desirable. The determination of B-oxybutyric acid in the blood would be of great value, but the methods now available are difficult and require a considerable amount of time. On the whole the determination of the carbon dioxide content of the alveolar air bids fair to prove one of the most useful aids in judging of the severity and course of acidosis. It is comparatively simply done, and it gives accurate information of the conditions which prevail in the blood at any given time. The presence of a positive ferric chloride reaction in the urine shows that abnormal acids are being formed, but if at the same time the alveolar air remains normal it is probable there is no immediate danger to be feared. When the alveolar carbon dioxide falls below normal the danger zone is being approached. Values between 35 and 30 mm. may be taken as indicating the development of a considerable acidosis, and one that demands treatment, but they need not give rise to the fear of any serious complication. Carbon dioxide tensions between 30 and 20 mm. are of much more significance, and are to be regarded as evidence that the patient is nearing the border-line and must be watched with great care. A constantly falling carbon dioxide tension is a serious warning, and is of great prognostic value. If the carbon dioxide tension is down to 20 mm. or lower the patient has reached a state in which coma may suddenly appear. Indeed, Poulton<sup>13</sup> who has given this matter considerable attention, states that "values of below 2.5 per cent. (about 18 mm.) indicate the early onset of coma, possibly within forty-eight hours unless drastic measures are taken." Analyses of the alveolar air in a case which was recently admitted to the Peter Bent Brigham Hospital in diabetic coma showed that the carbon dioxide tension varied between 6 and 10 mm. Very similar figures are given by Poulton for his cases in coma.

Besides being an aid to prognosis the alveolar air determinations may be of distinct value as a guide to therapy. When alkali is being administered the urine gives little evidence as to the results that are being accomplished until its reaction has been changed. As has already been stated, the ferric chloride reaction often becomes more intense. The alveolar air, however, gives an accurate indication of the effect of treatment. As the acidosis is overcome the carbon dioxide tension rises until it reaches normal. At this point the patient is out of immediate danger, but frequent examinations will be necessary to keep one informed as to when vigorous treatment may have to be instituted again. This effect of the alkali is

<sup>13</sup> Proc. Roy. Soc. Med., 1914, vii (Med. Sec.), 171.

usually rapid and complete in cases of mild or moderate acidosis, but if the acidosis has developed to an extreme grade, a point is apparently reached beyond which the administration of alkali produces little or no permanent change in the clinical picture or in the composition of the alveolar air. Thus in the patient with diabetic coma mentioned above, in spite of the administration of considerable amounts of sodium bicarbonate, both by mouth and intravenously, no permanent beneficial effect was produced. On admission, shortly after he had gone into coma, the alveolar carbon dioxide was 6.71 mm. After vigorous treatment it rose to 10.7 mm. on the next day, and synchronous with this his mental condition improved so that he was recognizing his friends. On the following day the carbon dioxide tension was 12.9 mm. and there was further subjective improvement. During the night, however, his condition suddenly changed and he went rapidly into a diabetic coma in which treatment was without avail and which was fatal within twenty-four hours. It is, of course, possible that much larger amounts of alkali should have been given, and perhaps such treatment would be safe if it were guided by alveolar-air determinations.

**CHRONIC NEPHRITIS.** Among the many theories which have been brought forward to explain the clinical picture of uremia is that which accounts for it on the basis of an acidosis. As early as 1888 von Jaksch<sup>14</sup> suggested that this was the underlying factor. During the last few years this theory has again been brought into prominence by the work of Straub and Schlayer,<sup>15</sup> on the alveolar air in advanced cases of nephritis, and by the studies of Sellards<sup>16</sup> and Palmer,<sup>17</sup> both of whom showed that a mild grade of acidosis may be present comparatively early in the course of the disease. Evidence of the existence of an acidosis in moderate cases of chronic nephritis is based in large part on the so-called "alkali-tolerance" test of Sellards. If a normal individual be given sodium bicarbonate the urine will become alkaline after the ingestion of 5 grams or, at the most, of 10 grams. If an acidosis is present a much larger amount of alkali will be needed to produce this change in reaction. The probable explanation of this is that during the development of the acidosis the reserve supply of base in the tissues is being drawn upon to neutralize the acids which are produced. When more base is supplied to the body by the administration of alkali this is first used to restock the depleted stores in the tissues before it is allowed to accumulate in the blood and bring about a change in the reaction of the urine. If this theory of the mechanism by which the body disposes of alkali, when it is administered to it during acidosis is correct—and there is every

<sup>14</sup> *Ztschr. f. klin. Med.*, 1888, xiii, 350.

<sup>15</sup> *München. med. Wchnschr.*, 1912, lix, 569.

<sup>16</sup> *Johns Hopkins Hosp. Bull.*, 1912, xxiii, 289; *ibid.*, 1914, xxv, 141.

<sup>17</sup> *Med. Communication, Massachusetts Med. Soc.*, 1913, xxiv, 133.

reason to suppose that it is—then it will be seen that the “alkali-tolerance” test may serve as an important index of what may be termed “tissue acidosis.” Since the acid products of metabolism are largely formed within the cells, it is evident that “tissue acidosis” may occur before there will be any marked change in the blood. Probably only after large amounts of acid have been produced in the cells, and the supply of bases in the cells has been to a considerable extent used up, will unneutralized acid pass into the blood, and only after the blood itself has neutralized much of this will the composition of the blood be changed in the sense of an increased acid reaction. Thus quite a degree of acidosis may exist in the body without affecting the blood so as to cause a fall in the carbon dioxide tension of the alveolar air.

The “alkali-tolerance” test throws much light on the time of the development of acidosis in renal disease and on its underlying causes.<sup>18</sup> In early cases of nephritis, such as those in which the phthalein test shows a normal excretion, even when they are accompanied by a pronounced hypertension, it is unusual to find any evidence of acidosis. The urine is readily made alkaline by the administration of 5 to 10 grams of sodium bicarbonate. As cases become more severe and the phthalein excretion begins to drop below the normal level the “alkali-tolerance” test is likely to become increased, so that 15 to 20 grams of sodium bicarbonate are required to change the reaction of the urine. As the nephritis progresses and phthalein excretion continues to decrease the “alkali tolerance” rises until, in very advanced cases, it may be extremely difficult to administer sufficient base to make the urine alkaline. The development of the acidosis thus bears a definite relationship to the functional capacity of the kidney as indicated by the phthalein test. The fall in phthalein output runs fairly parallel with the rise in non-protein nitrogen content of the blood, and it is natural to refer both of these, and also the acidosis which accompanies them, to the decrease in the excretory power of the kidney. The acidosis of chronic nephritis is thus due to retention. While in diabetes the acidosis is the result of increased formation of acids, in nephritis it apparently depends on the inability of the organism to get rid of even a normal amount of acid. Whether there is also in nephritis a production of acids which exceeds the normal is as yet an uncertain question. The experimental work of Mosenthal,<sup>19</sup> which seems to show that a toxic destruction of protein is one of the accompaniments of nephritis, would favor such a view, for it is well known that proteids give rise to large amounts of acid-combustion products.

The urine in nephritis gives little information as to the acidosis within the body—even less than does the urine in diabetes. The

<sup>18</sup> Results to be published in detail in a separate communication.

<sup>19</sup> Arch. Int. Med., 1914, xiv, 844.

hydrogen-ion concentration may be high, but it rarely exceeds the normal limits, and high values are by no means constant. The ammonia in the urine may not be increased, and is a comparatively unimportant index, as much of it may be retained with the other nitrogenous decomposition products. The ferric chloride reaction if positive is usually weak. The acidosis of nephritis is not due to the acetone bodies, but as to what acids are retained in the body little is known.

While urine analysis is of limited significance in determining the grade and character of the acidosis in nephritis, much can be gained from observations on the alveolar air. A study of about 50 cases in all stages of the disease permits of several general deductions on the manner and extent of its development. In the early stages of the disease there is no accumulation of non-volatile acids in the blood such as to cause a deviation of the tension of the alveolar carbon dioxide from the normal. Even after the phthalein excretion falls below normal, and after the "alkali-tolerance" test shows evidence of a considerable degree of "tissue acidosis," there is rarely any change in the alveolar air. Insofar as the acids are not excreted by the kidney they are apparently taken up by the blood, but the amount is not sufficient to cause any change in the reaction of the blood. At the time when the phthalein excretion is very low, and more often when there is no phthalein excretion, one frequently begins to find a drop in the alveolar carbon dioxide tension. This, however, is not a constant finding, as one patient with no excretion of phthalein and with non-protein blood nitrogen up to 90 mg. per 100 c.c. of blood had an alveolar carbon dioxide tension of 40.3 mm. ten days before she died. The majority of patients have a slight or moderate decrease of carbon dioxide, with values ranging from 37 to 25 mm. Such figures may be found during the development of uremia, but when the condition advances to coma the acidosis is frequently of higher grade. Nevertheless, in advanced uremia the alveolar carbon dioxide may not be below 30 mm. One patient had a carbon dioxide tension of 33.8 mm. and another of 24.4 mm. on the day before death. In certain cases, however, the onset of uremia is accompanied by the occurrence of a sudden and severe acidosis. In two instances the carbon dioxide fell to 4.59 and 19.1 mm. respectively. Both of these patients presented the clinical picture which is seen in diabetic coma, and their respiration was increased so that it amounts to a true "air hunger." The former died on the day after the alveolar air was examined. The latter was unusually interesting in the response shown to alkali therapy. The patient was a woman, aged forty-five years, with a history of nephritis going back for several years. Her blood-pressure was about 200 mm., and the non-protein nitrogen in her blood had risen to 90 mg. per 100 c.c. of blood. For over a month the phthalein test had shown practically no

elimination of the dye in the urine. In spite of the very advanced nephritis her general condition remained fair, and except for headache there was no evidence of uremia until January 11. On this day she first began to complain of being short of breath. The alveolar carbon dioxide was 19.1 mm. tension. Turning over in bed caused marked dyspnea. Two days later, January 13, the patient was unconscious and her respiration was slow, but so deep as to be quite typical of "air hunger." The alveolar air was not taken at this time, but 300 c.c. of 4 per cent. sodium bicarbonate solution were given intravenously. On the following morning the carbon dioxide tension was 23.4 mm. This indicated a marked acidosis, and as the "air hunger" persisted, a further intravenous injection of 700 c.c. was given later in the day. When the patient was seen on the next morning the clinical picture had entirely changed. She was quite conscious, recognizing every one, but was greatly nauseated and looked very sick. The "air hunger" had disappeared, and the respiration was shallow, slow, and irregular, with rather prolonged periods of apnea. The alveolar carbon dioxide tension had risen to the normal value of 41.5 mm. On the next morning it had fallen to 36.9 mm. Respiration was perhaps slightly deeper, but did not suggest "air hunger." There were occasional deep, sighing breaths. Her sensorium was clouded, but she was conscious and responded fairly well to questions. In an attempt to ward off the further development of acidosis, 375 c.c. of 5 per cent. sodium bicarbonate were given intravenously, but in spite of this the alveolar carbon dioxide had next day dropped to 25.1 mm., her respiration was deeper and more rapid, and she was becoming unconscious again. On January 17 she was comatose and had begun to have convulsions. Respiration was deep, irregular, and stertorous. It was extremely difficult to get satisfactory samples of alveolar air. Those obtained showed a carbon dioxide tension of about 30 mm. Another intravenous alkali injection was without effect, and the patient died on January 18. This case is reported in considerable detail because it shows unusually well the development of a marked acidosis during uremia, which was clinically similar to the typical acidosis of diabetes. The existence of the acidosis was confirmed by the alveolar-air examinations, with its response to alkali treatment was, though temporary, most striking.

The demonstration of the occurrence of acidosis in chronic nephritis is a comparatively simple matter. It is much more difficult to form a correct opinion as to the part which the acidosis plays in the symptomatology of nephritis and of uremia. To do so on the basis of the knowledge now at our command would probably be impossible. So complex are the changes in the blood and tissues which may result from the inability of the kidneys to excrete the waste products of metabolism, and so many are the substances which may accumulate in the body, that it is not

easy to determine what effects any one of them may produce. However, in a condition like uremia it is most important to separate out the constituent causative elements, for only by so doing will its pathology eventually become clear. It is, of course, possible that the accumulation of acid and the consumption of the supply of base in the tissues, even as it occurs during the early period of retention, may have some abnormal effect on the fixed cells. If there is any such it is obscure, and at present there is no evidence as to how it acts. In the later stages, especially with the change in the blood and the fall in the alveolar carbon dioxide, the acidosis, as will be shown later, seems to bear a relation to the occurrence of dyspnea. The association of acidosis and uremia is of special interest. The extent to which acidosis appears in and causes the symptom-complex of uremia is a variable one, but it seems to be an element in most if not all cases. In one group of patients uremia may exist for a considerable period and the acidosis be of a grade that produces a high "alkali tolerance," but only a slight depression of the alveolar carbon dioxide. With the onset of coma the alveolar carbon dioxide will perhaps drop somewhat, but there is no development of "air hunger," nor does the carbon dioxide tension reach the values seen in diabetic coma. Other patients present a picture in which the acidosis is in the foreground. With the onset of severe uremia at or just before the time when coma sets in the clinical signs of acidosis present themselves, the respiration is similar to that in diabetic coma, and the alveolar carbon dioxide will be found to have dropped to the very low values which obtain in that condition.

The single experience cited above shows that this type of case will, at least sometimes, respond to alkali treatment. The response will probably only be temporary, for uremia is not acidosis alone, and even if the acidosis is successfully combated, there are other factors which must eventually bring about death.

**CARDIAC DYSPNEA.** Some of the newer methods for studying the physiology of the respiration have also been applied in an attempt to explain the etiology of cardiac dyspnea. While there are as yet many points that are uncertain, progress has been made, and the facts so far determined are of importance to the clinician. Lewis, Barcroft, and their collaborators were the first to point out that in considering this problem one must recognize two groups of dyspneic patients. One of these consists of the pure cardiac cases. "These are usually young subjects with fresh or heightened color, and although cyanosis—slight, moderate, or deep—is present, dyspnea, as indicated by the rate of respiration, is not great. The respirations range from twenty-five to thirty-five per minute; orthopnea is present and the field of respiratory response is strictly limited."<sup>20</sup> The other group consists of elderly subjects with con-

<sup>20</sup> *Quart. Jour. Med.*, 1915, viii, 97.

tinuous dyspnea, often intensified for short periods, especially at night, without marked cyanosis, with Cheyne-Stokes breathing, an increased pulse rate, and a subnormal temperature. The clinical picture is essentially what is generally known as cardiorenal disease. Further studies have confirmed the desirability of differentiating these two groups, partly on account of their clinical symptomatology and partly because the cause of the dyspnea is not quite the same in both classes.

The group of pure cardiac cases with dyspnea consists chiefly of patients with valvular disease and acute decompensation. They are often extremely breathless when first brought to the hospital, but it is quite striking that severe dyspnea does not generally persist for long. After one or two days the respiration usually becomes much quieter, although orthopnea may continue for some time. While dyspnea is produced by very slight exertion, they are comparatively comfortable as long as they are at rest in bed. In an attempt to obtain some information as to the cause of the dyspnea in this group of cases the alveolar carbon dioxide has been studied and the following facts obtained. At a time when the patients show no dyspnea while they are at rest, even though very slight exertion causes breathlessness, the alveolar air is perfectly normal. Very frequently during the period of dyspnea the alveolar carbon dioxide shows no evidence of acidosis. Indeed, the absence of acidosis is, according to Lewis and his associates, one of the characteristics of this type of case. Since they have failed to find any evidence of acidosis by using Barcroft's method for the blood, and since the dyspnea and the cyanosis seem to them to run nearly parallel, they believe that the dyspnea depends on poor oxygenation of the tissues. The studies at the Peter Bent Brigham Hospital, however, have demonstrated that in many cases at the time when the dyspnea is most severe the alveolar air analyses show a depression of carbon dioxide tension such as indicates a moderate grade of acidosis. Thus, two patients who entered the hospital with severe dyspnea and a high degree of cyanosis showed carbon dioxide tensions of 30.9 and 34.7 mm. respectively. A few days later, when they had regained compensation, the alveolar air had returned to normal. It is noteworthy that the phthalein tests, the non-protein nitrogen in the blood, and the blood-pressure were normal in these patients, so there is nothing to make one believe that there was any renal element in the case. These observations on the acidosis of cardiac dyspnea confirm the results of Beddard and Pembrey<sup>21</sup> and of Porges, Leimdörfer, and Markovici.<sup>22</sup>

Thus in the pure cardiac cases dyspnea may be present when the alveolar carbon dioxide is normal or when it is somewhat

<sup>21</sup> British Med. Jour., 1908, ii, 580.

<sup>22</sup> Ztschr. f. klin. Med., 1913, lxxvii, 446.

depressed. In other words, there may or may not be acidosis, and if there is any acidosis, it is usually present only during the very acute stage, after which it quickly disappears. In either case the dyspnea is probably correctly explained by Lewis as the result of insufficient oxygenation of the tissues. With the failing heart and slowing of the circulation, carbon dioxide may accumulate in the respiratory centre and stimulate it to increase the ventilation. If the condition of the circulation becomes so poor that the amount of oxygen reaching the tissues is greatly reduced there will be incomplete combustion of the substances formed during cellular metabolism and the accumulation of acids in the blood. These acids, acting as a stimulus to the respiratory centre, will increase the pulmonary ventilation so that the carbon dioxide tension will be reduced and the oxygenation of the blood will be improved. Since the kidneys are normal the excretion of acid will go on rapidly, and as soon as the circulation has readjusted itself the excess of non-volatile acids will be got rid of. Then the alveolar air will return to normal. In cases with sufficient passive congestion, however, to inhibit the renal functions, there may well be some temporary retention of acids.

The second type of dyspneic patients consists of those in whom the element of acidosis plays a more significant part. Lewis recognizes that in this group renal lesions are generally present and believes that the acidosis is connected with nephritis, but he apparently feels that the evidence is as yet too scanty to allow of their being definitely associated together. Our own studies have been on cases in whom the renal condition has been investigated as carefully as possible. Blood-pressure, phthalein tests, and determinations of the non-protein nitrogen of the blood all support the view that these are usually cases with extensive degenerations of the kidneys. Clinically, the patients are frequently elderly persons, often with the pallor of arterial or renal disease, with comparatively little cyanosis. Orthopnea is present, and particularly characteristic are sudden attacks of severe dyspnea occurring especially at night. The respiration is usually rather rapid, shallow, irregular, and very frequently Cheyne-Stokes in character. The patients are often dull or sleepy, dosing off during the periods of apnea, arousing suddenly, and sometimes having great distress during the periods of dyspnea. The urine is that of chronic nephritis and the blood-pressure is usually well above normal. The condition is most often a permanent one, lasting days, weeks, and even months before death. Less often there are transient or fairly prolonged intervals of a return to comparative comfort and health. In general, the condition indicates serious organic disease and the prognosis is bad.

Analysis of the alveolar air in this clinical condition shows that



it is quite generally associated with a fall in the carbon dioxide tension. This decrease is not great, however, and the values, while sometimes reaching as low as 25 mm., are most frequently between 35 and 30 mm. In almost all the cases in which the symptom-complex has been clear cut and the acidosis evident the functional tests have shown that the kidneys were decidedly inefficient. Usually the phthalein output was measured as "traces" or "zero." It is thus quite natural, and probably correct, to conclude that the acidosis is due to an accumulation depending on incomplete excretion, and is of renal origin.

It is extremely difficult to decide how important a part the element of acidosis plays in producing the clinical symptoms of dyspnea in cardiorenal disease. In another clinical condition, such as diabetes, the same amount of acidosis as indicated by the alveolar air produces no gross changes in the respiration. In diabetes it is only when a much greater depression of the alveolar carbon dioxide has taken place that the breathing is affected, and even then a wholly different type of respiration results. The deep, regular respiration of diabetic acidosis is totally unlike the shallow rapid, irregular, periodic respiration of cardiorenal disease. If then the dyspnea of cardiorenal disease depends on acidosis alone it must be that there are other factors which modify the way in which the organism reacts. On the other hand, because the acidosis is not very great, one must not necessarily conclude that it is of no significance in the production of the dyspnea. Some observations recently finished indicate that it is of considerable importance.<sup>23</sup> Subjects have been allowed to breathe through valves attached to a so-called "closed-circuit apparatus." The expired air passes through two tanks and is subsequently rebreathed, so that the inspired air has a continually increasing content of carbon dioxide. By special arrangements the pulmonary ventilation of the subject is measured, and samples of the inspired air are taken at regular intervals for analysis. It has been found that normal individuals react in a fairly constant manner to the stimulus of the carbon dioxide in the inspired air. Thus when the carbon dioxide reaches a concentration of between 4.5 and 5.5 per cent. of the inspired air, the subjects are breathing so deeply that their initial ventilation has been doubled. Patients with cardiac disease, but who are compensated while at rest, react in a similar manner. Patients with decompensated cardiorenal disease, however, and with acidosis as indicated by the alveolar air, are much more sensitive to the carbon dioxide, and it is found that their ventilation may become doubled with only 2 or 3 per cent. carbon dioxide in the inspired air. It has already been shown that owing to the peculiar com-

<sup>23</sup> To be reported in detail in a separate communication.

position of the blood it can take up a great deal of acid without having its reaction perceptibly affected, but beyond a certain point, the mechanism fails, and the addition of even small amounts of acid affects the reaction noticeably. Here is the apparent condition in the patients with acidosis. The blood has already taken up all the acid it can without having its reaction affected, so that the addition of even small quantities, as in breathing the air containing carbon dioxide, makes a shift in the blood reaction and increases the pulmonary ventilation. The same result would undoubtedly be brought about if the carbon dioxide were produced in the body, as by muscular exercise. The amount of muscular work which would suffice to produce dyspnea would be much less than normal. Thus, while the degree of acidosis which is present in cardiorenal disease is usually insufficient to cause the changes in respiration which one is accustomed to associate with acidosis, or indeed to account for the dyspnea alone, it is undoubtedly an important element. It renders the organism unusually sensitive to any added production of acid, and would, in all probability, accentuate the effect on the respiration which might be produced by an inefficient heart.

## HISTORICAL SKETCH OF THE DEVELOPMENT OF THE DUODENAL TUBE.<sup>1</sup>

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IN connection with duodenal feeding let me sketch the development of the duodenal tube.

Shortly after the stomach pump was discovered by Kussmaul examination of the gastric contents became of great importance for the diagnosis of diseases of the stomach. As soon as physicians appreciated the value of the stomach tube it was felt it would be desirable to be able to examine also the secretion of the organs farther down, particularly the pancreas, because it was known the pancreas is of much greater value to the process of digestion than the stomach. But at first this wish—namely, to reach the secretion and analyze it—appeared to be impossible of fulfillment.

<sup>1</sup> Lecture delivered at the New York Post-Graduate Medical School, 1915.

For a number of years the first attempt to reach the pancreatic secretion was abandoned until Boas,<sup>2</sup> about 1889, published a paper in which he said that he had succeeded, by the introduction of a stomach tube into the fasting stomach and massaging the liver, in obtaining a fluid from the stomach which was regurgitated there from the duodenum. It gave the reaction of the pancreatic secretion. While it is possible, in rare instances, to succeed in bringing on such a regurgitation in the fasting condition, it is naturally not a procedure that can be done in a routine way. If there is, for instance, gastric juice in the stomach already the results will be vitiated.

The second step was undertaken by Boldyreff,<sup>3</sup> a Russian physician working in the laboratory of Professor Pawloff. He noticed on animals with gastric fistulae that when they were given oil or fat a regurgitation from the duodenum into the stomach took place, and he suggested to make use of this phenomenon for clinical purposes. Volhard<sup>4</sup> then applied this test in practice. He gave oil or butter and half an hour later washed out the stomach. This method also is not applicable to all cases. In many regurgitation does not take place, or the regurgitated matter is mixed up with gastric juice, and is of no value.

Other more direct attempts have been made to obtain the duodenal secretion.

In 1897 Hemmeter<sup>5</sup> described a method by which he thought he could introduce instruments into the duodenum. A brief consideration of the construction of his instrument will make it clear that it is difficult to accomplish with this apparatus what Hemmeter claims.

Hemmeter's instrument consists of a rubber bag that resembles the stomach, and this bag contains in its upper segment a groove or a canal for another tube which is inserted into the duodenum through the pylorus as soon as the bag has been introduced and had been filled with air.

The trouble with this instrument is that stomachs vary in size and configuration. One can not obtain in advance a mould of any particular stomach, so that the bag will tally exactly with the shape of the stomach, and therefore it is impossible to say whether the opening of the groove in the bag is really opposite the pylorus. After the bag is in the tube is pushed down, and Hemmeter says

<sup>2</sup> Ueber Darmsaftgewinnung beim Menschen, Centralblatt f. klin. Med., 1889, No. 6, p. 97.

<sup>3</sup> Der Uebertritt des natürlichen Gemisches aus Pankreassaft, Darmsaft und Galle in den Magen, Pflüger's Arch. f. Physiol., 1908, p. 13.

<sup>4</sup> Ueber die Untersuchung des Pankreassaftes beim Menschen und eine Methode der quantitativen Trypsin bestimmung, Münch. med. Wchnschr., 1907, p. 403.

<sup>5</sup> Versuche über Intubation des Duodenums, Archiv f. Verdauungskr., 1897, Bd. 2, p. 85.

that he then succeeds in pushing the tube into the duodenum through the pylorus. I do not know, whether he succeeded or not. Hemmeter asserts that he obtained pancreatic secretion. This, however, is no proof that the secretion came from the duodenum through the tube, but I assume, rather, that he got it from the stomach. I do not believe it is easy to obtain pancreatic secretion by Hemmeter's instrument. The second clinician to try to reach the duodenum directly by means of instruments was Kuhn.<sup>6</sup> This was about one year later. He constructed tubes with a metal spiral inside. The spiral served to prevent too much bending and kinking and doubling upon itself. He then took a long stomach tube, put the metal spiral inside and manipulated it for a long time, until he thought he had reached the duodenum. He also maintained that he did get the pancreatic secretion. X-ray examination was not yet in vogue and so could not confirm the position of the tube in the duodenum. Kuhn's tube did not differ much from a stomach tube. I also experimented with it, but never succeeded in entering the duodenum with it. It certainly was a difficult procedure, both for the physician and for the patient. It is impractical.

After the publication of Kuhn's article Hemmeter gave up the use of the bag and tube and used Kuhn's instrument. This was the way things stood for a number of years. Then gradually I evolved the present instrument from various experiments and procedures that I will now give in detail.

I tried to find a method of testing the motor function of the intestines. For this purpose I<sup>7</sup> made use of porcelain beads, sifted the stool, and observed the time it took for them to reappear in the stool. This was described about eleven or twelve years ago.

Later, I desired not only to test the motor but also the digestive functions of the stomach and intestines. Various test substances (as meat, catgut, potato, fat, etc.) were attached to little beads.

The question now came up whether the digestion of the various test substances took place in the stomach or in the intestines.

In order to differentiate this,<sup>8</sup> I gave patients beads with test substances attached to a thread, arranged so that the thread was about 53 cm. long, so that the beads could not reach the duodenum. After four to five hours I pulled up the thread and looked whether the substance was still left. I worked with beads and thread so that the beads could not pass the pylorus. Thus I found which of the substances was digested entirely in the stomach. Those test substances which remained intact in the stomach but were missing

<sup>6</sup> Sondierungen am Magen, Pylorus und Duodenum des Menschen, *Archiv f. Verdauungskr.*, 1898, p. 19.

<sup>7</sup> *Diseases of the Intestine*, 1904, 2d edition, p. 62.

<sup>8</sup> A New Method of Testing the Functions of the Digestive Apparatus, *Med. Record*, February 10, 1906.

on the beads when found in the feces must, therefore, have been digested beyond the stomach—in the intestine.

A short time later, while dealing with the question of the patency of the pylorus, I conceived the idea of giving beads to see whether they would pass the pylorus, in order to thus measure its permeability. This paper was published in 1908.<sup>9</sup>

The digestive test capsule as it is now made consists of the test substances all attached to beads, which again are held together by a silk string, the beads will reappear in the stool together, and we can then see which of the test substances have been digested and which have not.

In order to know whether the pylorus was permeable I had to have some substance which would change when it reached the duodenum and would not change in the stomach.

I attached to the thread one bead and a little bag containing a piece of dimethylamidoazobenzol-agar—the idea of using agar was to have a firmer substance than, for instance, test paper, so that the change of reaction should not take place too abruptly, but should proceed slowly.

Attach to the thread one bead at thirty inches from the lips, with dimethylamidoazobenzol agar, another one at twenty inches, likewise with dimethylamidoazobenzol agar, which latter can not reach the duodenum. The two beads are put in a gelatine capsule and given to the patient. Six hours later the beads are withdrawn and inspected. This should be done at a time when there is presumably free HCl present in the stomach, as for instance, one hour after Ewald's test breakfast. If the two beads are in the stomach, both will be red. If one was in the duodenum and one in the stomach the duodenal bead will be yellow and the other red. If we find that both are red, or that the lower one is red, we may suspect that there exists some obstruction at the pylorus to the passage of the beads from the stomach into the duodenum.

As soon as I noticed that we could enter the duodenum with the thread and the bead, I thought that it would be better to have a capsule or little bucket instead of the bead, as it could bring us the duodenal fluid itself.

That gave me the idea of the duodenal bucket (Fig. 1). If it is found that the bucket is filled with contents of an alkaline reaction containing pancreatic ferments, we know that we have been in the duodenum. Roentgen-rays confirmed that the duodenal bucket really was in the duodenum. This was described by me<sup>10</sup> in an article entitled "A New Method of Estimating the Permeability of the Pylorus and an Attempt at Testing the Pancreatic Function Directly."

<sup>9</sup> A New Method of Estimating the Permeability of the Pylorus and an Attempt at Testing the Pancreatic Function Directly, New York Med. Jour., June 20, 1908.

<sup>10</sup> Loc. cit.

As soon as I saw that we could enter the duodenum with this instrument I had the desire to do something more for the pylorus or duodenum. I<sup>11</sup> constructed an instrument that could be pushed over the thread. This was a thin catheter, by means of which I obtained duodenal juice. The thread served as a guide to enter the duodenum. Not only can we aspirate the contents of the duodenum by the introduction of a catheter, but by means of another specially constructed instrument we can dilate the pylorus (October, 1909).

Taking into consideration that the introduction of this catheter instrument was not very agreeable to the patient, and that it could not enter deep into the duodenum, I soon afterward had the idea of employing simply a small rubber tube ending in a perforated

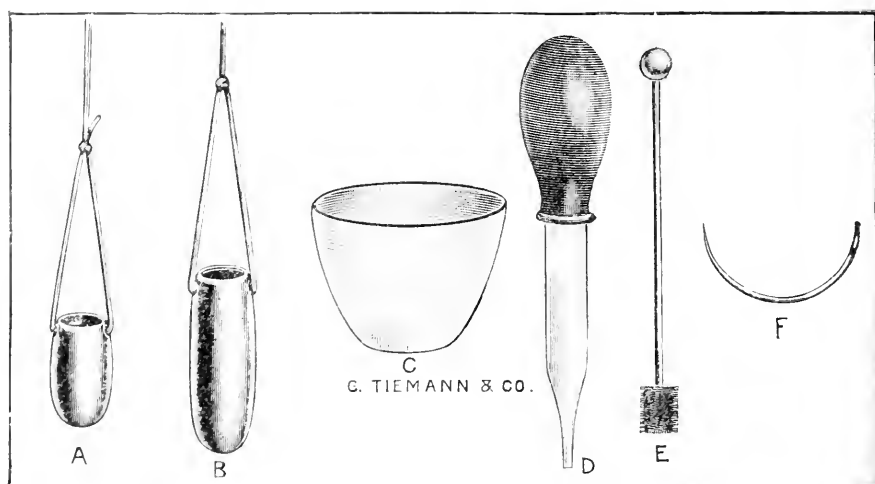


FIG. 1.—The duodenal bucket and its accessories. A, small size; B, larger size; C, porcelain dish; D, aspirating pipette; E, brush; F, needle.

metal capsule, which may be given instead of the bucket, letting the stomach do the work of introducing it into the duodenum. This is the main principle—instead of pushing an instrument to let the stomach carry out the work. This principle was of the greatest value. That led me to the construction of the duodenal pump, so-called because I first used it to aspirate the duodenal contents. It consists of a moderately thin rubber tube, at the end of which is attached a perforated olive. If the rubber tube is too thin, it is difficult to obtain the fluid; if too thick, it is too clumsy and not so pleasant for the patient.

<sup>11</sup> Max Einhorn, A New Method of Catheterizing the Pylorus and Duodenum, Medical Record, October 9, 1909.

This method was demonstrated by me<sup>12</sup> on a patient at the meeting of the Clinical Society of the Physicians of the German Hospital

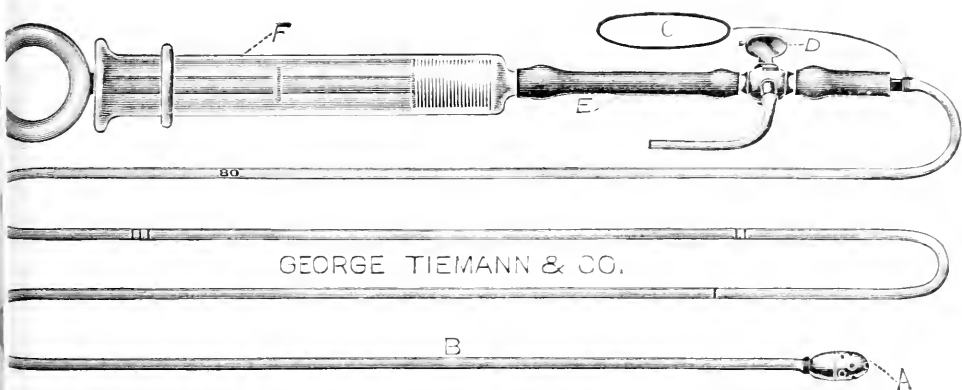


FIG. 2.—The duodenal pump. A, metal capsule, lower half provided with numerous holes, the upper half communicating with tube B; I, II, III are marks 40, 56, and 70 cm. respectively from capsule; C, rubber band with silk attached to end of tubing, which can be placed over the ear of patient; F, aspirating syringe; E, collapsible connecting tube; D, three-way stopcock.

of New York, on November 11, 1909. There were about fifty practitioners present.

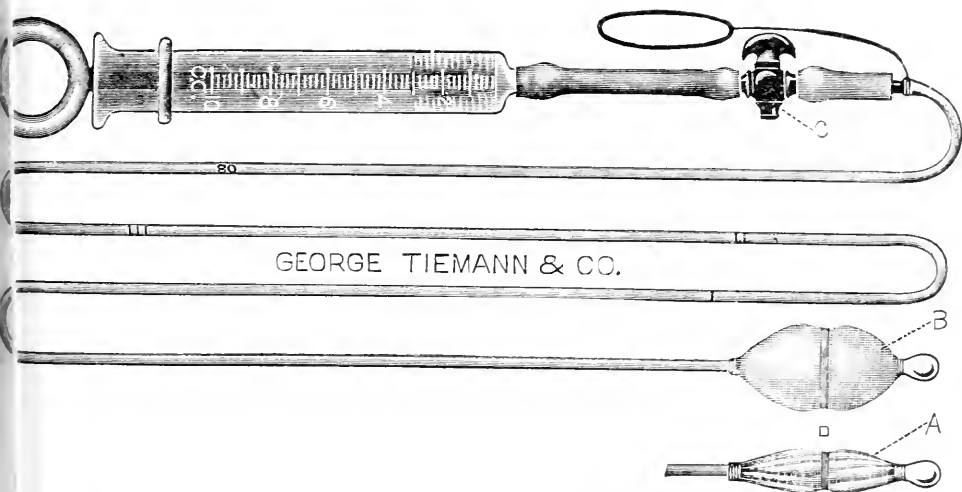


FIG. 3.—Pyloric dilator. A, rubber bag with gauze envelope in collapsed shape; B, rubber bag with gauze envelope, when inflated with air; C, stopcock.

As soon as I had the pump my desire was to treat obstruction of the pylorus without operation. There is a great deal of danger

<sup>12</sup> Max Einhorn, A Practical Method of Obtaining the Duodenal Contents in Man, Medical Record, January 15, 1910.

attached to operations on the pylorus. Extreme dilatation of the stomach is caused at times not so much by a real stricture, as by a spasm of the pylorus, as described by me and demonstrated at autopsy. There may be pylorospasm without obstruction. I saw the good results obtained by stretching in cardiospasm and thought that similar results could be obtained in pylorospasm.<sup>13</sup> I constructed an instrument on a similar principle (Fig. 3).

The next point was that if we have the duodenal contents and can stretch the pylorus, we can also use the instrument for treatment.

One can now handle duodenal affections the same as gastric conditions.

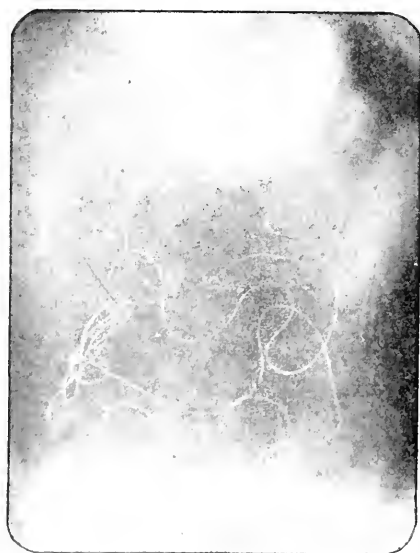


FIG. 1. —Roentgen-ray photograph of patient K, with the Intestinal Delineator in the digestive tract, shortly after bismuth ingestion into the stomach. The course of the intestine is seen for about nine feet beyond the pylorus. I am indebted for this beautifully-executed Roentgen-ray photograph to Dr. W. H. Stewart, who took it for me at the German Hospital.

As soon as I had the duodenal pump, a physician consulted me, who was vomiting everything and could not be nourished by rectum, because of diarrhea. I used the tube for examination, and had the idea instead of taking out the tube, to leave it there and to employ it for nutritive purposes. I did so for ten days. He now feels well, having no trouble whatever. This was first done in December,

<sup>13</sup> Max Einhorn, Dilatation of the Stomach and Chronic Benign Ischochymia, Illinois Med. Jour., June, 1910.



1909. January, 1910, I<sup>14</sup> demonstrated this first patient with duodenal feedings before the Clinical Society of the German Hospital.

Now I will give you a few points by which to determine whether the tube is in the stomach or duodenum. If you aspirate and find that the fluid comes out quickly, looks watery, HCl present, Congo paper turns blue, dimethyl paper red, litmus paper red, then you know that it is in the stomach. If, on the contrary, you get only very little fluid, of neutral or alkaline reaction, and yellow color, then you know that you are in the duodenum. Sometimes a patient has no HCl in the gastric contents; how will you then know? There are two additional ways by which this may be determined: (1) by the way it is obtained, as shown by the extremely slow flow of the fluid, and (2) by giving the patient a colored liquid which he has not before had, either milk or raspberry syrup. Have the patient drink some milk and aspirate: if the milk is not obtained immediately after drinking it will be known that you are in the duodenum. To prove this still more conclusively, pull the tube up farther until you are in the stomach and then again aspirate, when you will obtain the milk that the patient has just swallowed. If the patient has had milk before the test, you can make use of raspberry syrup instead as an indicator. This test is more positive than an *x*-ray, but if desirable an *x*-ray may also be made.

How far can one go into the intestinal tract? I am grateful to Dr. McCafferty for consenting to have me test this on him. Now that the principle of allowing the natural forces to push the bucket along is recognized as correct, obviously there is no limit to letting it go as far as it wishes. The deepest I have gone is about nine feet beyond the pylorus. The deeper the bucket goes down the more, of course, the difficulty of pulling it up increases. I have an *x*-ray picture showing this (Fig. 4). We can undoubtedly enter still farther, only we must be careful that the tube does not curl up in the stomach.

We now have a clear conception of this instrument, and the new field it opens, in which one can study the pylorus, duodenum, gall-bladder, liver, pancreas, etc. I do not doubt that our advance in the study of digestive disorders will be most important along these lines.

<sup>14</sup> Max Einhorn, Duodenal Alimentation, Med. Record, July 16, 1910.

## TONSILLAR ENDAMEBIASIS AND THYROID DISTURBANCES.

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A CONSIDERATION of the literature on the causation of endemic goitre emphasizes very strongly the wide diversity of theories on this subject. The recent tendency has been leading away from the older chemical theories, and the idea of an infectious nature of the causative agents has been advanced. Specifically among such investigators, McCarrison<sup>1</sup> and Farrant<sup>2</sup> have, in the last two years, outlined a groundwork for the future studies on the bacterial toxic origin of thyroid overgrowth. McCarrison in a study of endemic goitre in India determined that the stools of goitrous subjects contained an infective agent by his ability to reproduce the clinical picture of goitre in test animals through the ingestion of this material. Raw water, particularly that containing slime from wells, etc., was held to be infected because of the production of goitre in men from a non-goitrous region when used by them. Boiling or filtering through a Berkefeld filter rendered the same water innocuous. He concluded from this evidence that a mineral substance is not the causative agent and that a bacterial origin is logical; and his results from the use of intestinal antiseptics add weight to the theory of an intestinal origin of the supposedly causative bacterial toxins. Farrant advanced the first definite evidence of a specific bacterial agent. In his earlier report, from his results of experimental inoculations and autopsies, he assigned various infections of the body to three groups in their relation to the thyroid: (a) those having no effect, (b) those that induce chronic or colloid goitre, and (c) those that produce complete or acute hyperplasia. It is only in Farrant's later work, however, that he proposes the theory and evidence of a mutant colon bacillus in the intestinal tract as an important factor in goitre production. The constant finding of this coliform bacillus led him to the belief that its prolonged ingestion in contaminated waters is a cause of endemic goitre through its production of a toxin which on absorption influences the thyroid. The suppurative streptococci and staphylococci, according to Farrant, fall into the group of non-

<sup>1</sup> London Lancet, January 18, 25 and February 8, 1913.

<sup>2</sup> British Med. Jour., February 28, 1911; *ibid.*, July 18, 1914.

thyrotoxic bacteria, but *Micrococcus catarrhalis* is given a high place in the production of thyroid-stimulating toxins. As bearing upon the body of the present paper it may be mentioned here that while the location of the infection concerned in the production of such toxins is not an essential feature, Farrant is inclined to believe that pyorrheal conditions play a more important part in nature than do tonsillar infections.

Halstead,<sup>3</sup> in a reconsideration of the experimental side of the study of the relation of general and focal infections to thyroid enlargement, lays considerable emphasis upon infection being involved as a natural causative agent. Billings<sup>4</sup> urges a relationship between tonsillar focal infections and thyroid enlargement. Beebe<sup>5</sup> has made the relationship between pathological conditions of the nose and throat and hyperthyroidism the subject of a recent paper, in which attention is called to the fact that 40 per cent. of hyperthyroid patients in his experience give a history of repeated attacks of acute tonsillitis. He urges attention, likewise, to the care of upper respiratory conditions in the prevention of the subsequent development of hyperthyroidism. Norregard<sup>6</sup> reports an even higher grade of relationship, having uniformly found in a group of 35 thyroid cases some definitely infected lesion, usually in the tonsil. He refers to the anatomical relationship of the tonsils and thyroid in support of the suggested connection, and relates a complete recovery in one case after tonsillectomy, with improvement in other cases in which treatment was directed to similar conditions.

The interesting fact of the occurrence of acute thyroid hyperplasia in infants in Brazil (in the disease known as *opilação*) through the local infestation of the gland by a protozoan parasite, *Schizotrypanosoma cruzi* Chagas, which later proceeds into chronic goitre with cretinism if life persist, should be called to mind in the same general relation. It is true the recent work of Marine<sup>7</sup> and of Cannon, Binger, and Fitz<sup>8</sup> do not sustain this belief in the infectious origin of goitre, but neither in full sense eliminates the possibility of its importance. Marine in his more recent work on goitre in brook trout, following up the work of himself and Lenhart on this subject, fails to sustain the belief in its infectious origin; but concludes that in fish goitre is a non-infectious, non-contagious, symptomatic manifestation of a fault of nutrition, the exact biochemical nature of which is not known. In a series of feeding experiments a highly artificial diet of liver was apparently the major etiological factor, which could be corrected at once by the use of the whole sea fish as food. The kinetic theory of the causation of exophthalmic

<sup>3</sup> AMER. JOUR. MED. SCI., January, 1914.

<sup>4</sup> Jour. Amer. Med. Assn., September 12, 1914.

<sup>5</sup> Ibid., August 29, 1914.

<sup>6</sup> Ugeskrift for Laeger, Copenhagen, January 14, 1915, lxxvii, No. 2, p. 51-74; abst. Jour. Amer. Med. Assoc., February 27, 1915.

<sup>7</sup> Jour. Exper. Med., January, 1914.

<sup>8</sup> Proc. Amer. Physiol. Soc., Amer. Jour. Physiol., March, 1915, p. 363.

goitre<sup>9</sup> would seem to receive additional weight from the experiments of Cannon, Binger, and Fitz, who, working on the theory that repeated emotional disturbance may lower a high neuron threshold and thus give rise to far more stimulation than normally, fused the anterior root of the right phrenic nerve of a cat with the right cervical sympathetic cord. With regeneration even the ordinary stimulus of normal breathing would stir up a volley of impulses in the superior cervical sympathetic ganglion. In the period from May to October, in four of six cats surviving operation they noted in one cat an increase from the normal 165 pulse beats per minute to 222, in others diarrhea and falling out of the hair of the neck and back, generally an unusual extreme excitability, and in one exophthalmos. In a word, by experimentally lowering a high neuron threshold in the sympathetic nervous system the typical picture of so-called exophthalmic goitre may be produced. From this study Jonnesco's work in the removal of the superior cervical sympathetic ganglion receives a degree of substantial support as an extreme surgical measure.

If the older classification of goitre be narrowed by the exclusion therefrom of enlargements of the thyroid gland which are of neoplastic nature and those dependent upon simple hyperemia, edema, hemorrhage, or upon suppurative changes, the remaining examples may be grouped in two classes: the first characterized by more or less active hyperplastic features of a simple or combined type, the second including chronic sclerotic, calcific, and atrophic parenchymatous changes as the main features (usually with accumulation of colloid in excess). While a relation between these two groups is by no means demonstrably clear, there are cases seen from time to time in which the sequence of early and progressive enlargement with symptoms of dysthyroidism into chronic enlargements with symptoms of hypothyroidism and with the type of histological changes of the chronic group is evident. It is theoretically conceivable that every case of chronic goitre has been preceded either by a frank stage of hyperplasia or by one of such gradual and insidious type that its clinical recognition has not been realized. It is at least permissible in our present uncertainty to tentatively adopt such view as a working theory, and to hold that in searching for a cause or for the causes of goitre the greater chance of success attends the close investigation of this supposedly constant but uncertain stage of active hyperplasia. Nor is it likely, when we appreciate that histological evidence indicates that the type of hyperplasia is not uniform, that the etiology is either simple or that the probable multiple causes are uniform in all cases. There are cases (the exophthalmic type) in which the hyperplasia concerns mainly, and to a marked extent, the lining cells of the follicles,

<sup>9</sup> Chile, AMER. JOUR. MED. SCI., January, 1913.

causing a moderate enlargement of the gland bulk, and a large occupation of the acinous spaces by the enlarged and multiplied cells at the expense of the ordinary colloid contents, and with changes in the appearance of this substance. On the other hand (parenchymatous goitres) the hyperplasia may in other instances involve the development of new acini and the enlargement of the existing ones with no important change in the size and appearance of the lining cells and with a general increase of the ordinarily appearing colloid. This latter form suggests strongly a true hypertrophy of the gland, such as would be called forth by some increased demand for its usual and full function. Or, as a third type, the hyperplasia may concern itself more particularly with the interglandular connective-tissue stroma, at times with and at other times without prominence of attendant vascular growth (leading into the fibrous and vascular goitres). In ordinary occurrences a given hyperplastic goitre may present any one of these types in predominance, or combination may be met with in which the histological pictures may vary among themselves and perhaps vary in different fields of observation of the same specimen.

If these variations are significant they argue best for the multiplicity of specifically operating causes, suggesting, on the one hand the likelihood of such examples of apparently pure hypertrophy as are seen in parenchymatous goitre, a general hyperplasia called forth by some demand for increased thyroid function, and, on the other hand, of stimulation to special cellular growth of the parenchyma (as in the exophthalmic type), of the connective-tissue framework (acute hyperplastic interstitial thyroiditis), or of the vessels (vascular goitres), by some selective agency operating directly upon these elements.

That special functional activity may be called forth indirectly, particularly in experimental conditions, by nervous stimulation is by no means inconceivable; and such an interpretation the writers are disposed to raise in explanation of the results of Cannon, Binger, and Fitz above referred to. (Here, too, one may conceive of the influence of emotion and of excess of sympathetic stimulation by hyperactivity of the adrenal and other chromaffin tissues.) All of our evidence of the purposes of thyroid function in life would indicate that it serves multiple objects in the economy, so that in selecting its undoubted but relatively poorly understood antitoxic or detoxifying importance in illustration of the argument the field of this line of consideration is by no means exhausted. We believe commonly that as an antitoxic organ the thyroid is efficient mainly through its iodothylin secretion, probably largely by the iodine moiety of this molecule. One may well fancy, as has repeatedly been suggested, that some toxic substance (its precise character and its origin, whether inorganic or organic, whether exogenous or endogenous, being immaterial for the immediate

purposes of argument) which has a strong affinity for iodine may be constantly introduced into the economy from the ingested water or food or manufactured in the course of metabolism, or generated by microbial agencies here or there in the body; that such substance is, therefore, constantly robbing the economy of its iodine, and that in response the thyroid as the important iodine-secreting organ is called into particular activity to acquire and secrete iodine to replace this loss. Here might well fall the cases of apparent dietary fault (as those of Marine), or if there be a chemical fault in the water of *kropf-brunnen* (a view almost abandoned), it might well operate along such line; and here, too, if infection be, as is so frequently suggested, of importance one may be tempted to suspect that the toxins of the infection, irrespective of the site of the infection (only holding the likelihood of its persistence and of the continuity of toxin formation), may align themselves, having some special fixing ability of the iodine of the thyroid secretion and coming into contact with the latter either in the thyroid or in the general system as the case may be. Ordinarily the result of such a scheme should be a simple hypertrophy, but there can be for the present, at least, little objection to the supposition that excessive demand might induce even the marked cellular hyperplasia of the exophthalmic type of goitre.

If, on the other hand, we admit the possibility of some selective stimulus to growth of one or other of the histological elements of the gland (notably, of course, the lining follicular cells), we at once should be disposed to attribute high prominence to agencies located in the gland or in such anatomical relation as to easily and in concentration arrive in the gland. This opens at once the infective possibilities and the local disturbances of surgical operation on the gland, recalling directly the possible involvement of the thyroid in *opilação*, the active cellular hyperplasia met in the remnants of the gland tissue when partial ablation of the thyroid is performed, and the variable hyperplasia met about foci of frank infection of the thyroid by suppurative bacteria. But there is no question of the usual rule of failures to demonstrate any type of microorganisms in the tissue of these hyperplastic thyroids, and one is disposed, therefore, to appeal strongly to the influence of toxins carried by as direct a route and in as concentrated quality as possible from extra-thyroid foci of infection to the gland. Here particularly may be assigned the frequent coincidence of various infective lesions of the mouth (pyorrhea), the tonsils, and the upper respiratory tract; the close lymphatic relation of the upper parts of the lateral lobes, as shown by Ehrhardt,<sup>10</sup> with the submaxillary and sublingual glands, being probably the route of admission of the supposed toxins to the organ. Stress has been laid more than once

<sup>10</sup> Beitr. z. klin. Chir., xxxi.

upon a relation between infections in the mouth and nose, and the writers present further evidence below of such relation; nevertheless, it should be emphasized that this cannot be regarded as excluding infections elsewhere from a similar relation (provided the toxins from that infection be thyroselective). Nor do the writers in the least care to be interpreted as holding goitre to be invariably the result of infection or the effect of infective toxins. But as one type of agency, either by calling out special thyroid activity or by direct selective stimulation to hyperplasia, infections or their toxins may perhaps be regarded as a factor in goitre production; along with nervous influences, the poisons of faulty alimentation and metabolism, as well as other possible factors. So far as the type of infection is concerned we would believe with Farrant that microörganisms (and their toxins) are in some degree selective, some not influencing the thyroid at all, others calling forth parenchymatous cellular growth and multiplication, still others inducing proliferation of the elements of the stroma, etc., and that in the matter of location no appropriate infection can be excluded; but the closer the focus and the more free and direct the mode of convection, the more pronounced and frank the effect is likely to be in the thyroid gland.

Several years ago some of us undertook a statistical study of endemic goitre in Wisconsin in connection with the work of the Medical Clinic in the University at Madison, with particular reference to evidence of its development in relation to preceding or coexistent infectious affections of the nose and throat.

Wisconsin's situation in the glacier zone with its geographical position in the goitre belt furnishes a fertile field for the study of endemic goitre. Some idea of the frequency of its occurrence can be gained from the following data obtained from the physical examinations of men and women entering the University of Wisconsin from 1910 to the fall of 1914 inclusive:

TABLE I.

Total examined.			Goitre.				Dysthyroidism.			
Year.	Total.		Men.		Women.		Men.		Women.	
	Men.	Women.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
1910	819	512	140	17.1	217	42.3	4	0.5	2	0.4
1911	772	298	126	16.4	136	45.6	7	0.9	4	1.3
1912	1049	427	238	22.8	225	52.8	6	0.5	35	8.4
1913	1315	543	424	32.2	247	45.0	4	0.3	18	3.3
1914	1328	569	362	27.2	271	47.6	5	0.3	8	1.4

Taking the examinations of 1914, the following table (Table II) outlines the relative frequency of involvement of the different lobes of the thyroid in men, together with the pathological changes in the nose and throat found associated with these thyroid dis-

turbances. Of the 1328 men examined, 362, or 27.2 per cent., had thyroid involvement, and to this group the following figures pertain:

TABLE II.

		Cases.	Percentage.
Simple goitre involvement	Both lobes and isthmus . . . . .	169	46.6
	Both lobes . . . . .	38	10.4
	One lobe and isthmus . . . . .	42	11.6
	Isthmus . . . . .	57	15.7
	Right lobe . . . . .	34	9.3
	Left lobe . . . . .	17	4.6
Dysthyroid involvement	Both lobes and isthmus . . . . .	5	1.3
	Total . . . . .	362	
Pathological changes in nose and mouth	Nasal . . . . .	80	22.0
	Cryptic tonsils . . . . .	6	1.6
	Cryptic and nasal . . . . .	77	21.2
	Fibroid and hypertrophied tonsils . . . . .	25	6.9
	Nasal, fibroid, and hypertrophied tonsils . . . . .	140	38.6

22.8% }  
90.3% }

Without entering into a discussion of the details of this table a glance will impress the very marked prevalence of anatomical morbid changes in the tonsils and nasal passages in the group, a total of over 90 per cent. of the goitrous individuals showing such defects. It should be observed that only those changes which are resultant from a single long-continued or repeated inflammatory attack in the nose and throat are here included; and without possibility of histological classification the arrangement of the goitres has been simplified into two groups: those without symptoms or signs of thyroid intoxication being classed as simple goitres, and those showing undoubted constitutional symptoms of disturbed thyroid secretion as dysthyroid types.

The accumulated data of preceding years' investigation afforded decided evidence of the actuality of a connection between these nasal and throat affections and the large occurrence of thyroid involvement. The recognition of the tonsils as a site of parasitism by *endameba gingivalis* (Gros), in the laboratories of the Universities of Pennsylvania and Wisconsin raised the question of a possible connection of this organism with the thyroid enlargements in consonance with the evidence then attained of its importance in the etiology of pyorrhea and its probable importance in certain examples of chronic tonsillitis, and in various systemic complications, as arthritis, anemia, neuritis, etc.<sup>11</sup>

<sup>11</sup> Cf. Barrett, *Dental Cosmos*, August and December, 1914; Smith, *Dental Cosmos*, September, 1914; Bass and Johns, *New Orleans Med. and Surg. Jour.*, November, 1914; Smith, Middleton, and Barrett, *Jour. Amer. Med. Assn.*, December 14, 1914; Evans and Middleton, *Jour. Am. Med. Assn.*, January 30, 1915 et al.



Two possibilities of etiological connection of these parasites with thyroid hyperplasia were considered: (*a*) direct extension of the protozoa from the mouth or nose or throat to the thyroid and parasitism of the organ by the amebæ, and (*b*) the effect of toxins arising from the symbiosis of the amebæ and their many bacterial associates upon the gland. The first was *a priori* held as improbable, because surely these organisms would long since have been detected in the course of histological study of early goitres. Nevertheless, a number of at least comparatively early specimens of hyperplastic goitres were examined with this point in view, without in any instance recognizing amebiform cells in the tissue. With the belief, however, that the second of these possible connections might be correct, a plan of study was projected and pursued.

The writers regret that, owing to the dominating thought of the importance of tonsillar involvement at first, this report fails to include pyorrhea as one of the sources of toxic substances suspected by them of being involved in thyroid complication of nose, mouth, and throat infections. This fault in reality, however, weakens only the statistics of coincidence and does not in any way militate against the force of the results reported. Moreover, in the future this may be easily, and probably with much profit, be corrected in certain work now in progress upon the general subject. Here, too, the writers are anxious for clarity to urge that in suggesting endamebiasis of these upper respiratory and mouth parts as one of a number of possible causes of thyroid hyperplasia they are not advancing these protozoa themselves as the specific producers of the toxins effective in producing the hyperplasia. If this were true there is no reason why everyone who is the host of these parasites (a high proportion of all adults) should not also be the subject of thyroid enlargement. Our belief is, that the essential toxic factors are really the products of the bacteria associated with the amebæ, and that these bacteria are the variants and the amebæ are the constants in many varying infections of the mouth, tonsils, and the nasal passages and sinuses; that there is a symbiotic relation between the protozoa and the bacteria, the amebæ by proteolysis of various cells producing a pabulum of special value for the nutrition and growth of the bacteria, and the bacteria being constantly ingested and digested by the amebæ; that as one particular form of bacteria is prominently present its toxin is liberated in prominent amount when the bacterial cells are thus digested; and that if that toxin has selective stimulative effect upon the thyroid elements, thyroid hyperplasia will follow (as, following to Farrant, if there be a high proportion of *Micrococcus catarrhalis* present in the amebic lesion in the tonsils, for example, the toxin carried by lymphatic drainage into relation with the thyroid will stimulate the thyroid parenchymatous cells to growth and proliferation).

In prosecution of the study a series of 34 of the above (Table II)

goitre subjects with chronic cryptic tonsillitis were selected for further examination. Material was aspirated from the pouting crypts with a glass pipette bent toward the end and drawn out to a smooth point, a rubber bulb being attached. This material was mounted on a warmed slide, mixed with warm normal saline solution, covered, and examined immediately on the warm stage. Myriads of bacteria, spirilla, numerous granular leukocytes (pus cells), erythrocytes and a few epithelial cells constitute the ordinary findings. In 33 of the 34 cases examined, *endameba gingivalis* (Gros) was found present.<sup>12</sup> That in the course of this study 15 cases with chronic cryptic tonsillitis were also met with the same amebæ in the contents of the tonsillar crypts, but without thyroid enlargement is to our minds no indication, in the absence of knowledge of the bacterial associates with the amebæ in each individual case, that in the first group the thyroid changes were independent of the endamebiasis.

This group includes 25 individuals with simple goitre (11 women and 14 men) and 9 persons (5 women and 4 men) showing symptoms of dysthyroidism. In order to obtain some degree of evidence of a relationship amounting to more than mere coincidence between the tonsillar foci of symbiotic infestation and the thyroid changes, emetin hydrochloride was administered hypodermically to 23 of these 34 individuals. This mode of approach is, of course, an empiric one, and by no means ideal; but, as stated in a previous report,<sup>13</sup> "the application of a specific drug for the relief of a supposedly specific infection is an acknowledged therapeutic principle. The further application of this principle to the relief of remote conditions complicating the original specific lesion is justified." The general data of the entire group, with a statement of the thyroid involvement, the details of emetin treatment of 23 of the cases, and the results of such treatment, are presented in tabulated form for the sake of brevity in Table III.

The details of the administration of emetin hydrochloride were quite variable, that is, although the subcutaneous or intramuscular route was constantly used, the dosage and the number and the interval between the series of injections varied within rather wide limits. The period of observation ranged from two weeks to seven months. Reëxamination of the material from the tonsillar crypts after the use of emetin was made in but 16 of the 23 cases. Of these, in 13 reëxamination showed a disappearance of the endamebæ, a result in general conformity with the disappearance of tonsillar endamebæ previously noted by us<sup>14</sup> on the administra-

<sup>12</sup> Seven more cases of cryptic tonsillitis with thyroid involvement have shown endamebæ in the cryptal contents, bringing the total up to 40 positive cases out of 41 examined.

<sup>13</sup> Evans and Middleton, Jour. Amer. Med. Assn., January 30, 1915.

<sup>14</sup> Smith, Middleton, and Barret, *supra cit.*

TABLE III.

No. and sex.	Involvement.	Dysthyroid symptoms.	Tonsillar and anclae.	Emetin hydrochloride treatment.	Time interval.	Amelae.	After treatment.	Symptoms.
1 M.	Right lobe	Tachycardia; tremor; dysphagia.	+	3 series: 7, $\frac{1}{8}$ gr.; 3, $\frac{1}{4}$ gr.; 2, $\frac{1}{2}$ gr.; 1, $\frac{1}{4}$ gr.; 7, $\frac{1}{8}$ gr.	5 mos.	+	Unchanged	Less nervous; no tremor; pulse fell from 96 to 84. (No goitre mass).
2 M.	Both lobes and isthmus	Exophthalmos; von Graefe, Moebius	+	1 series: 7, $\frac{1}{8}$ gr.	1 mo.	+	Reduced $\frac{1}{2}$ "	
3 F.	Both lobes and isthmus	Tachycardia; fainting spells	+	3 series: 4, 1 gr. each	6 wks.	-	Reduced $1\frac{1}{2}$ "	Psychic improvement.
4 M.	Both lobes and isthmus	None	+	None				
5 F.	Both lobes and isthmus	None	+	None				
6 M.	Both lobes and isthmus	None	+	None				
7 M.	Both lobes and isthmus, acute	None	+	2 series: 7, $\frac{1}{8}$ gr.; 2, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.	5 mos.	-	Reduced $\frac{1}{2}$ "	
8 F.	Right lobe and isthmus	Exophthalmos; tremor; tachycardia	+	5 series: 2, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.; 3, $\frac{1}{2}$ gr.	5 mos.	-	Reduced $1\frac{3}{8}$ "	Marked improvement in all symptoms.
9 M.	Left lobe and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.	3 wks.	-	Unchanged	
10 F.	Right lobe and isthmus	None	+	2 series: 4, 1 gr.; 1, $\frac{1}{2}$ gr.	1 mo.	-	Reduced $1\frac{1}{2}$ "	
11 M.	Both lobes and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.	6 mos.	-	Reduced $\frac{1}{2}$ "	
12 M.	Both lobes and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.				
13 M.	Both lobes and isthmus	Tachycardia; tremor; exophthalmos; von Graefe	+	None				
14 M.	Both lobes and isthmus	None	+	None				
15 M.	Both lobes and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.	2 wks.	-	Reduced $\frac{3}{8}$ "	
16 F.	Both lobes and isthmus	None	+	3 series: 1, $\frac{1}{2}$ gr.; 1, $\frac{1}{2}$ gr.; 1, 1 gr.	6 wks.	-	Reduced $\frac{1}{2}$ "	
17 M.	Both lobes and isthmus	Atypical	+	2 series: 2, $\frac{1}{2}$ gr.; 3, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.; 2, $\frac{1}{2}$ gr.	5 wks.	?	Unchanged	Unimproved.
18 F.	Both lobes and isthmus	None	+	3 series: 1, $\frac{1}{2}$ gr. each	6 wks.	-	Reduced $\frac{1}{2}$ "	
19 M.	Both lobes and isthmus	Nervousness	+	None				
20 M.	Both lobes and isthmus	Tremor; nervous; tachycardia	+	3 series: 4, $\frac{1}{2}$ gr. each	2 mos.	-	Reduced $1\frac{1}{2}$ "	Unchanged.
21 F.	Both lobes and isthmus	Tachycardia	+	3 series: 2, 1 gr.; 1, $\frac{1}{2}$ gr.; 3, 1 gr.; 2, 1 gr.	2 mos.	-	Unchanged	Marked improvement.
22 M.	Both lobes and isthmus	Tremor; fainting; lateral nystagmus	+	None				
23 F.	Both lobes and isthmus	Tachycardia; tremors; exophthalmos	+	None				
24 M.	Both lobes and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.	2 wks.	-	Reduced $\frac{1}{2}$ "	
25 M.	Both lobes and isthmus	None	+	1 series: 7, $\frac{1}{8}$ gr.	1 mos.	-	Reduced $\frac{1}{2}$ "	
26 M.	Both lobes and isthmus	None	+	4 series: total, 6, $\frac{1}{2}$ gr.	5 mos.	-	Reduced $\frac{1}{2}$ "	
27 F.	Isthmus	None	+	1 series: 4, $\frac{1}{2}$ gr. each	2 mos.	-	Reduced $\frac{1}{2}$ "	
28 F.	Isthmus	Tremor; tachycardia; faint; exophthalmos	+	5 series: total, 7 gr.	1 mos.	-	Reduced $\frac{1}{2}$ "	Pulse fell from 120 to 88; improved in every way.
29 F.	Both lobes and isthmus	None	+	5 series: 7, $\frac{1}{8}$ gr.; other 4, $\frac{1}{2}$ gr.	6 mos.	-	Reduced $1\frac{1}{2}$ "	
30 F.	Both lobes and isthmus	None	+	2 series: 4, $\frac{1}{2}$ gr.	6 wks.	-	Reduced $\frac{1}{2}$ "	
31 F.	Both lobes and isthmus	None	+	5 series: total, 6+	7 mos.	-	Reduced $1\frac{1}{2}$ "	
32 F.	Both lobes	None	+	None				
33 F.	Both lobes and isthmus	None	None	None				
34 F.	Both lobes and isthmus	None	+	None				

tion of emetin in certain arthritides complicating tonsillar endamebiasis. Twenty-two of the 23 treated have been under general observation since the beginning of treatment. Of these, 18 have shown a reduction in the circumference of the neck averaging about three-fourths of an inch (greatest reduction in Case 8, exophthalmic goitre, one and five-eighths inches; no reduction appreciated in 4 cases; in no case was there enlargement). Such changes in size of a goitre form, it is true, but a crude measurement of the influence of treatment; but the absence of fluctuations approaching or above their untreated state is to our minds more than of passing interest. Fluctuations are quite common among untreated cases, and fluctuations were met by us in 3 cases of goitre with acute upper respiratory infections under treatment in the group now under discussion, but in none was there any close approach to the condition existant before treatment. The measurements were made from a constant point just above the seventh cervical vertebra posteriorly around the neck over the most prominent point of the goitre mass anteriorly, in order to avoid error in the individual case. Seven of the 9 cases of dysthyroidism of the general group were included among the 23 cases treated with emetin, and showed varying degrees of improvement in their symptoms (in no case was there advance noted in the severity of the usual symptoms; in several the symptoms almost or quite disappeared under treatment, and have remained so). While precaution was constant to prevent psychic influence, this factor cannot be excluded in 3 of the cases. In fact, in no case was reference made to the real object of treatment except as an effort to clear up a tonsillar condition; the measurements of the neck and the changes in the size of the same were, with but few exceptions, treated as mere incidents.

In analysis of these results, which show primarily an extremely high proportion of positive finding of endamebae in the tonsillar crypts in goitre subjects having, as is very frequently the case, chronic hypertrophic tonsillitis, and secondarily the frequent coincidence under treatment with emetin hydrochloride of (*a*) disappearance of the amebic parasites (with amelioration of the tonsillitis) and of (*b*) reduction in the size of the goitre and improvement in, or disappearance of, nervous and circulatory symptoms of dysthyroidism, brief attention should be further directed, perhaps, to the question of reduction in the goitre mass. The possibility of reduction to any degree must depend in the individual case upon the nature of the goitre. It could scarcely be expected in old fibroid or calcified goitres or in cystic goitres that the same degree of diminution in size could be attained (if any) as in goitres of recent enlargement closely connected with functioning excess. In the latter the removal of an exciting focus of toxin formation should be far more effective than in the former where permanent organic changes have been established; and in a general way the above tabulated results

indicate this in the more marked improvement met in the exophthalmic cases (as well in dysthyroidic symptoms as in the proportionate reduction in the goitre mass). From time to time, too, the question whether emetin does not possess a vasoconstricting action arises. Were this true it might be thought that reduction in the size of the goitre may, in part at least, be due to this factor. The rather ill-defined work of Muriel<sup>15</sup> reported early this year on the action of emetin constitutes the only assertion of such vasoconstricting influence of the drug as far as our present knowledge extends. Sollman,<sup>16</sup> on the other hand, attributes to the remedy a vasomotor paralyzing action, with fall of blood-pressure, in experimental animals; and all of the individuals in the present group whose blood-pressure has been followed (8) showed a very decided fall in both systolic and diastolic pressures. Studies now in course of completion at the University of Wisconsin on the vasomotor action of emetin hydrochloride under Dr. A. S. Lovenhart would indicate that the primary effect of the drug in test animals is a very transient vasoconstriction, succeeded by a definite dilatation of the vessels. Further studies with the plethysmograph on the effect of emetin hydrochloride on isolated organs are under way. From such data it would seem highly improbable that the reduction in the size of the goitres under observation by us could have resulted from a vasomotor influence of the remedy. Moreover, the uniformly maintained reduction over a number of months rather argues against so transient a matter as vascular constriction from vasomotor influence. We would prefer to believe, as above suggested, that the reduction noted in the goitre mass, as well as the amelioration of the dysthyroidic symptoms, is the result of the removal by emetin of the amebæ demonstrated in the tonsillar crypts in these cases, this resulting in a breaking of an important symbiotic chain of endamebæ and thyrotoxic bacteria, and removing thereby from these foci the active elaboration of the directly influential toxins. That absolute proof of this relationship is lacking we freely acknowledge, but believe there is more than mere suggestive value in the following conclusions which can be offered from the above.

CONCLUSIONS. 1. Tonsillar lesions of an infective cryptic character were found in 22.8 per cent.; and nasal together with tonsillar lesions existed in 90 per cent. of 362 goitrous individuals examined from this stand-point.

2. In typically diseased tonsils, out of 34 cases examined microscopically, 97 per cent. were found to harbor endameba gingivalis (Gros) in the tonsillar crypts.

3. Of 16 individuals of this group who after treatment by means of emetin hydrochloride were reexamined, 13, or 81 per cent., were shown to no longer have endamebæ in the cryptal contents.

<sup>15</sup> Clinical Med., February 1, 1915.

<sup>16</sup> Text-book of Pharmacology, ed. 1906, p. 309.

4. In 23 individuals to whom emetin was administered a reduction in the bulk of the goitre was appreciable in 18 individuals; and of 7 dysthyroid cases included in this group of treated cases 6 were benefited in degrees varying from slight amelioration to apparent cure.

5. Inability to demonstrate endamebæ in the thyroid gland renders improbable any direct causal relation of the amebic infestation of the tonsils *per se* upon the development of thyroid disturbances.

6. However, the improvement, morphologically and symptomatically, in the treated cases leaves little doubt, after ruling out a vasomotor influence from the emetin employed, as to an indirect relationship. A symbiosis of endamebæ with appropriate bacteria, leading to the elaboration and absorption into the thyroid of selective thyrotoxic poisons, is at least conceivable in explanation of such relation.

7. In no sense do the writers care to be understood as advancing hereby an exclusive explanation for all goitres; other types and other locations of infections capable of producing thyrotoxic toxins, perhaps, too, toxic substances having a similar influence but derived from metabolic or alimentary fault, or even entering the body from without, are all of possible influence; nor is the influence of sympathetic stimulation, however accomplished, to be overlooked. The writers are unable to follow, moreover, in any of these lines of thought, into any satisfactory explanation of the known occurrence of belts of endemic goitre along certain well-defined glacier drifts.

We desire to express our appreciation to Doctor R. H. Jackson, of Madison, for gross specimen of goitre and to Doctors Van Valzah, Rinker, and Morris, of the clinical staff of the University of Wisconsin, for kind coöperation in this study.

## PATHOGNOMONIC ALTERATIONS OF THE CEREBROSPINAL FLUID IN SYPHILIS OF THE NERVOUS SYSTEM.<sup>1</sup>

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THE cerebrospinal fluid of healthy individuals has a fairly constant constitution. Although we do not know its origin or its functions, we know that it is subject to alteration of constitution in many diseases, and especially in diseases of the central nervous system. Much study has been made to determine the specificity of such

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alteration—that is, whether there occur pathognomonic alterations of the cerebrospinal fluid. It need not necessarily show abnormality in any disease. It is usually altered in disease of the central nervous system, caused by pathogenic organisms (*Diplococcus intracellularis*, tubercle bacillus, poliomyelitis organism, *Treponema pallida*, etc.). It is most constantly altered in syphilitic diseases of the central nervous system. In the majority of such diseases, it is altered in a characteristic way, and in some the alteration is so constant and unvarying that it may be considered pathognomonic. When the syphilitic disease of the central nervous system is predominantly of the meninges and bloodvessels, that is, when the brunt of the lesion is borne by the connective-tissue structures, the change in the cerebrospinal fluid is subject to wide variation, depending upon the intensity of the infection, the rapidity and extent of the pathological process, and upon the individual (vital resistance).

**MENINGEAL SYPHILIS, CEREBROSPINAL SYPHILIS.** When the pathological process is confined largely to the meninges, the circumvascular spaces, and the bloodvessels the most conspicuous alteration in the cerebrospinal fluid in addition to the positive Wassermann reaction is an increase of the cellular elements of the fluid and particularly an increase of the mononuclear cells. If this increase amounts to 100 or more the cubic millimeter, and the polynuclear variety of cells are above 10 per cent., it may be assumed with much confidence that the syphilitic process is predominantly meningeal, it matters not what the clinical display is. If the fluid with these characteristics does not reduce Fehling's solution and shows no excess of globulin the assumption is even more certain. Furthermore, it is likely that such cases will yield promptly to appropriate treatment, inasmuch as the pathological alteration in the cerebrospinal fluid can be quickly brought, approximately, to a normal state. Of a large number of cases to bear out these statements I quote two:

**CASE I.**—Female, thirty-eight years old; married. There is no history of syphilitic infection; she has borne three children and four miscarriages. Complaint: breaking pains in arms and legs, headache, insomnia, nausea, occasional vomiting, indigestion, constipation. Duration of symptoms, eighteen months. Has been constantly under treatment for dyspepsia.

*Physical Signs.* Liveliness of the tendon-jerk; tremor of the outstretched fingers and of the lips.

	Sept. 2, 1912.	Sept. 16, 1912.	Nov. 20, 1912.
Serum, Wassermann . . . . .	+	+	—
Cerebrospinal fluid, Wassermann . . . . .	+	+	—
Cells (180 polynuclears) . . . . .	1480	149	5
Globulin . . . . .	+	+	—
Fehling's . . . . .	—	—	+

CASE II.—Male, aged twenty-six years; unmarried; became infected with syphilis one month before he consulted me for the relief of headache, spasm of the left side of the face and left upper extremity, lethargy, stuporousness, dysarthria, and anarthria. The evolution of these symptoms occurred in three months. Physical examination was negative, save for a slight paresis of the motor branch of the right fifth and of the seventh cranial nerves. Laboratory examinations.

	Oct. 7, 1913.	Oct. 20, 1913.	Oct. 31, 1913.	Dec. 9, 1913.	Dec. 22, 1913.	Mar. 17, 1914.	June 5, 1914.
Serum, Wassermann	++	+	—	+	—	—	—
Cerebrospinal fluid, Wassermann . . .	+	+	+	+	—	—	—
Cells (12 polymor- phonuclears) . .	533	171	70	34	16	12	5
Globulin . . . .	+	+	—	+	—	—	—
Fehling's. . . .	+	+	+	+	+	+	+

He received nine intravenous injections of salvarsan within two months and was then given salicylate of mercury hypodermically.

THE SEROLOGY OF ONE HUNDRED AND SEVENTEEN CONSECUTIVE CASES OF CEREBROSPINAL SYPHILIS. Examination of the blood serum of patients with that form of syphilis of the nervous system in which the brunt of the lesion is borne by the connective tissues of the central nervous system, shows that the Wassermann reaction in the blood serum is positive in 88 out of the 117 cases; the cerebrospinal fluid Wassermann is positive in 33 cases; and there is an excess of globulin in 46 cases. The cases were distributed as follows:

Serum (Wassermann).	Cerebrospinal fluid (Wassermann).	Globulin cases.	
+	+	+	23
+	+	—	6
—	+	+	3
—	+	—	1
		—	33
+	—	—	46
+	—	+	13
—	—	+	7
—	—	—	18
		—	84

Forty-six of the 117 show a positive Wassermann in the serum and a negative cerebrospinal fluid with a normal cell count.

In 23 of these cases no cells were found, in 16 not over ten cells, in 4 not over twenty cells, while 2 cases had a cell count between twenty and thirty cells.

The next largest group of cases, namely, 23—is that in which the serology is positive throughout and in which there is either a moderate or a marked pleocytosis; 11 of these 23 cases had a cell count of more than one hundred, while it ranged between ten and eighty cells in 12 cases; 2 of these cases showed the largest cell count obtained in any of the cases, namely, 1882 and 1630 respectively.



In 18 of the total of 117 cases the serology was negative throughout. In 5 of these cases there were no cells: in 8 between ten and twenty cells, and in the remaining 5 the cell count ranged between thirty and one hundred and fifty. In 13 of the total number of cases the serum Wassermann and the globulin were positive, while the Wassermann in the cerebrospinal fluid was negative. In this group of cases a moderate pleocytosis is the rule: 1 case had no cells, 3 not over ten, 2 not over twenty, 3 not over thirty, 2 between thirty and fifty, while 2 cases have over one hundred and two hundred cells respectively.

In 7 cases positive globulin was the only positive serological finding; while in this group the cell count ranged between ten and fifty cells, there was 1 case which showed over two hundred cells. In 6 cases both the serum Wassermann and that of the cerebrospinal fluid was positive, while the globulin test was negative. Only 1 of these cases had more than ten cells. In 3 cases the serum Wassermann was negative, while that of the cerebrospinal fluid and the globulin was positive; 1 of these cases had not more than ten and 2 not more than thirty cells. In 1 case only was the Wassermann of the cerebrospinal fluid the only positive feature of the serology. The cell count was not over fifty.

**THE CEREBROSPINAL FLUID IN TABES.** The cerebrospinal fluid taken from individuals whose brain and spinal cord display the reactions to the *Treponema pallida* that are known as general paresis and tabes is characteristically altered in from 60 to 75 per cent. of them.

The typical serological picture of tabes is: serum, Wassermann, +; cerebrospinal fluid, Wassermann, +; cells, 20 to 100; globulin, - + (usually -); Fehling's, +.

Increase of lymphocytes is the most constant alteration of the cerebrospinal fluid of individuals with tabes. In 200 consecutive cases, 154 had cellular abnormality of the fluid. In 30 instances the number of cells to the cubic millimeter of fluid was under five, and in 16 of these there were no cells. Of the 154 cases there were 23 which had upward of one hundred cells to the cubic millimeter. Such cases we are accustomed to designate hyperlymphocytic tabes, and we have learned that they are more amenable to treatment than the hypolympocytic varieties. Polynuclear elements in the spinal fluid of this variety of tabes is the exception, not the rule. The highest count in any patient of the two hundred consecutive cases was 592. There were 50 instances in which the count was about sixty and 122 instances in which it was about twenty-five.

We have never observed a case of hyperlymphocytic tabes with one thousand cells to the cubic millimeter in the spinal fluid. The extreme limit of the pleocytosis observed is well within four hundred cells per cubic millimeter. The presence of polynuclear elements in the spinal fluid of this variety of tabes is rather the exception

than the rule. Whenever found this phenomena is to be considered of favorable prognosis. It must be emphasized at this junction that the irritation is responsible for the pleocytosis, whereas the spirochete *per se* is responsible for the positive Wassermann reaction. The one may be removed without in the least influencing the latter, so that we may therapeutically succeed in doing away with most, if not all, of the pleocytosis, leaving behind a Wassermann reaction which cannot be influenced under any circumstances. Such a case is the following in this communication.

**SO-CALLED WASSERMANN-FAST CASES.** A gentleman, aged forty-seven years, recalled when his recollection was refreshed, that when a youth he had preputial ulceration of some sort to which he gave no attention. Four months before consulting me he experienced a sensation of heaviness in the feet and legs and occasional shooting pains. His complaint when I saw him was: weakness of the legs and some awkwardness in his walking; cushion sensation under the balls of the feet, numbness in the peroneal region; occasional imperative desire to urinate. His physical signs were typical of tabes: serum, Wassermann, +; cerebrospinal fluid, Wassermann, ++; cells, 98; globulin, -; Fehling's, +.

From October, 1910, he received 18 injections of salvarsan, 24 injections of neosalvarsan, 5 injections of salvarsanized serum, and 46 injections of salicylate of mercury.

The serum Wassermann test made once a month remained positive up to May 29, 1915, when it was found negative for the first time and the cerebrospinal fluid was likewise entirely negative. His symptoms at this time practically disappeared and he was discharging the obligations of an exacting professional duty, that of a general practitioner of medicine. On August 7, 1915, the serum Wassermann was again +.

Out of the 200 cases there were 7 instances in which it was impossible to make the serum negative despite the most protracted administration of antisyphilitics.

One of the most extraordinary and inexplicable occurrences is the behavior of the cells in the cerebrospinal fluid in certain cases of tabes in active treatment. In several instances (the percentage of cases is not yet ready to report) the cells of the cerebrospinal fluid increase while the patient is having very active anti-syphilitic treatment. I publish the serological card of one patient to illustrate this:

	Serum (Wassermann)	Cerebrospinal fluid (Wassermann).	Ce'ls.	Globulin.	Fehling's.
May 3, 1915	+	+	1	-	+
May 27, 1915	+	-	12	-	+
July 8, 1915	+	+	3	-	+
Aug. 12, 1915	+	-	3	-	+
Oct. 18, 1915	-	+	20	-	+
Nov. 11, 1915	+	+	11	-	+
Nov. 23, 1915	+	+	6	-	+
Dec. 8, 1915	+	+-	270	-	+

In the interval that elapsed between the first day given above and the last, he received eight intravenous treatments of salvarsan, three intraspinal treatments of mercury, and eighteen intramuscular injections of mercury salicylate.

Clinically the patient made very striking improvement; from being absolutely bedridden, he was able to get about the hospital without other aid than that of a stick, and the pains, of which he previously complained bitterly, had practically disappeared.

The cerebrospinal fluid taken from individuals who have tabes reduce Fehling's solution in nearly every instance. In 12 cases only out of 200 consecutive cases did it fail to do so.

The globulin of the cerebrospinal fluid is increased in nearly 50 per cent. of the cases. So far I have not been able to associate the increase of globulin with any definite clinical type of tabes.

When studying the blood serum and cerebrospinal fluid of patients who have disease flowing from syphilis it is of the greatest importance to determine whether the patient has recently taken treatment that is known to deter the Wassermann reaction. I have gone through the histories of my cases with much care to determine this; 41 of the 63 cases whose serum gave a negative reaction had received mercury or salvarsan before coming under my observation; 22 of them had not.

Of the 27 patients whose Wassermann reaction of the cerebrospinal fluid was negative, 17 had received antisyphilitic treatment.

**TABES AND KNOWLEDGE OF SYPHILITIC INFECTION.** A study of these 200 cases of tabes throws interesting light on the incidence of tabes. The accompanying table sets this forth:

Males . . . . .	161	
Females . . . . .	39	
	—	200
History of infection—hard chancre . . . . .	108	
Soft chancre . . . . .	13	
Gonorrhea . . . . .	20	
	—	
	141	
Denied . . . . .	59	
	—	200
Treatment at the time of infection . . . . .	107	
No treatment . . . . .	93	
	—	200
Treatment later . . . . .	102	
No treatment later . . . . .	98	
	—	200

**THE SEROLOGY OF GENERAL PARESIS.** In 70 consecutive patients afflicted with general paresis, the majority of them in the early stage of the disease, and 58 of which were males and 12 females, the Wassermann reaction of the serum was positive in 47 instances, negative in 17, and refused or not recorded in 6.

The Wassermann reaction of the cerebrospinal fluid was positive

in 53 instances, negative in 7 instances, and refused or not recorded in 10 instances.

The cerebrospinal fluid showed an increase of the cellular elements beyond the normal in 52 instances, no increase in 9, and no record in 9. The highest cell count of any case was two hundred and seventy. There were 9 instances in which the pleocytosis was above one hundred and 16 instances in which it was above fifty. The average cell count was fifty-eight, though the majority of instances showed a pleocytosis of from thirty to fifty.

The globulin of the cerebrospinal fluid was increased in 45 instances, not increased in 15, and no record in 10.

The characteristic precipitation of colloidal gold occurred in 97 per cent. of the cases of paresis. It will be recalled that Szygmondi suggested the use of colloidal metals to determine the quality of protein substances, and Lange attempted to determine the nature of the protein substance in the cerebrospinal fluid by an elaborate series of experiments with colloidal gold. It is not apparent, however, in the work of Lange that he came to any definite conclusion concerning the nature of the protein in the spinal fluid. The precipitation that he obtained with the use of colloidal gold suggested to him that it would be of great value in detecting syphilis. We were unable to corroborate the claim that colloidal gold, used after the manner described by Lange, is to be depended upon as a detector of syphilis in general, but it is the most reliable and unvarying phenomenon of general paresis.

THE EFFECT OF TREATMENT UPON THE ALTERATION OF THE CEREBROSPINAL FLUID IN PARESIS. It goes without saying that the denial of syphilitic infection on the part of the patient who has general paresis has very little weight. In this series of cases it was admitted in 29 cases, denied in 25, and nothing known of such an occurrence in 13.

The results of treatment may be summarized in a sentence; although the constitution of the cerebrospinal fluid is modified in many instances by the administration of salvarsan and mercury, it was never made normal.

CONCLUSIONS. *Cerebrospinal syphilis* (lesion predominantly of the meninges, bloodvessels). The blood serum gives a positive reaction (if the patient has not been subjected to antisyphilitic treatment) in about 75 per cent. of the cases.

The cerebrospinal fluid, on the other hand, gives a positive Wassermann reaction in only about 30 per cent.

The most constant alteration is pleocytosis. It occurs in upward of 80 per cent. of the cases. In the vast majority of instances the cell count is less than 100 to the cubic millimeter, though it may be more than 2000. Although treatment (salvarsan, mercury) usually reduces the number of cells, it does not always do so. Occasionally the pleocytosis increased within forty-eight hours after treat-

ment. The predominating cell is the mononuclear, but the higher the cell count the greater the admixture of polynuclear elements.

The globulin content of the fluid is increased in about 45 per cent. of the cases.

The fluid of patients with cerebrospinal syphilis reduces Fehling's solution in about 95 per cent. of the cases, but this has practically no diagnostic value, as the fluid taken from patients who have any organic nervous disease does the same thing. When a fluid does not reduce Fehling's it will be usually found to contain a large proportion of polynuclear cells.

*Tubes.* Lymphocytosis is the most constant alteration of the spinal fluid (75 per cent.). The number of lymphocytes in some instances suddenly increases while the patient is under active treatment.

The next most constant alteration is a + Wassermann (73 per cent.). The globulin is increased in 50 per cent. of the cases.

*General Paresis.* The cerebrospinal fluid gives a + reaction in 80 to 85 per cent. of the cases; an increase of the cellular elements in practically the same percentage and globulin increase in about 65 per cent.

The colloidal gold test is positive in 97 per cent. of the cases.

## SPONTANEOUS PNEUMOTHORAX.

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PNEUMOTHORAX is always secondary to disease of the lungs or of the chest wall, and therefore is a complication and never a primary condition. As a rule the disease to which it is secondary is obvious, but occasionally the pneumothorax dominates the clinical picture and the primary condition is obscure and in a measure unimportant. Pneumothorax occurring when the lungs are relatively healthy may cause such trivial symptoms as to be entirely unsuspected and its presence be revealed in the course of a routine examination. Although the physical signs of pneumothorax are straightforward enough, still if one is off guard they may be overlooked or misinterpreted.

My own experience with pneumothorax, until I made the observations herein recorded, had been gained by encountering it in cases with gross and obvious pulmonary disease or after injury to the chest wall. In these instances the symptoms were marked and the physical signs, though interesting, still were quite clear and direct in their significance. I was unprepared, therefore, for the following observation, which aroused a keen interest:

CASE I.—A young man during a cold has sudden pain in the right side. A few days later, December 2, 1909, examination reveals a complete right pneumothorax. Uneventful recovery in six weeks. On November 4, 1910, after lifting a weight, pain in the left side. Examination reveals complete left pneumothorax. Uneventful recovery in four weeks. Recurrence of left pneumothorax on December 24, 1910. In October, 1913, cough, sputum, signs of tuberculous infiltration in both upper lobes; tubercle bacilli in sputum.

Dispensary No. 5074. A. G., white male, aged twenty-two years, elevator constructor, came to the Phipps Dispensary of the Johns Hopkins Hospital on November 12, 1909, complaining of cough and pain in the lower right side. His father had been killed in an accident, his mother was living and well. He had four brothers and one sister all living and well; no history of tuberculosis in the family.

Patient had always been a healthy man and had had no serious illness since childhood. He had been a hard worker, smoked moderately, and did not abuse alcohol. He had had a cough for two years, dating his illness from a cold which he had contracted at that time. He had never had any constitutional symptoms. A few weeks before coming to the hospital he had contracted a fresh cold, and since then his cough had been worse, and he had had some pain in the right side. His average weight had been 123 pounds. On admission the temperature was 98.2°; pulse 72; respirations 22; weight, 130½ pounds; height, 5 feet 5¼ inches. The note of the examination on admission is as follows:

Patient is a well-nourished man of healthy appearance; his skin is rather pale, but the mucous membranes are good color. Tongue is slightly coated; teeth are in bad condition and there is definite pyorrhea. The mucous membranes of the throat are reddened and the left tonsil somewhat enlarged. The cervical glands are palpable, but are not particularly enlarged. There is no general glandular enlargement. The chest is well formed, right clavicle a little more prominent than the left; movement somewhat restricted over the right side. Tactile fremitus well felt on both sides, more marked on the right than on the left. The percussion note is a little impaired above and below the right clavicle and in the supraspinous fossa and at the extreme base. A few fine rales and an occasional medium moist rale heard over the area of impairment. Heart: the point of maximum impulse is in the fifth interspace, inside the nipple line; sounds are clear. Abdominal examination shows nothing noteworthy.

December 4, 1909. Patient felt well until the afternoon of November 28, when upon stooping over he suddenly experienced a sharp pain in the right side, followed by shortness of breath. The shortness of breath was not urgent, but he could not walk a block without stopping to catch his breath. Since then he has had pain in the side constantly and is unable to lie on his back or on the right

side on account of the pain. The shortness of breath has continued but occurs only upon exertion.

December 2. It was noticed that the breath sounds were absent over the right side, but the examination on that date was incomplete and the true condition was not made out.

*Examination.*—The patient is perfectly comfortable and walks about the dispensary without the least sign of distress. Pulse 90, respirations 20. The chest well formed and fairly symmetrical; both clavicles are prominent, the right perhaps a little more so than the left; movement about equal on the two sides, a little less on the right, but the difference is not striking. Fremitus is better felt over the upper right back than on the left side, but elsewhere, though felt, is distinctly diminished as compared with the left. The percussion note is a little impaired above and below the right clavicle and in the interscapular area. Over the lower front, and particularly below the angle of the scapula, the note has a distinct hyperresonant quality. On the left the lower border of the lung, in the midaxillary line, gives an excursion of 6 cm. on deep inspiration. On the right the lower border of resonance extends to the level reached by the lung on the left on full inspiration, and this point shows no respiratory variation. When the patient lies down the hyperresonant quality of the percussion note over the front is still more marked than when he sits up. On auscultation the striking feature is the suppression of the breath sounds. They are everywhere audible, but very distant and faint. The voice sounds are somewhat diminished in intensity, but show no alteration in quality. The point of maximum impulse is in the sixth interspace outside the mammillary line, and there is no cardiac dullness to the right of the sternum; heart sounds are clear. The roentgenogram shows a complete right-sided pneumothorax, with marked dislocation of the mediastinum. The tuberculin tests—1 per cent. and 5 per cent.—conjunctival, and cutaneous tests are all negative; the sputum shows no tubercle bacilli.

December 14. Patient has been feeling much better; he has no pain now and can lie with comfort on the right side. He walks with little discomfort; he has a little cough and expectoration. Examination shows the point of maximum impulse to be distinctly farther to the right, in the sixth interspace, just inside the mammillary line, 8 cm. from the median line. The percussion note is not so hyperresonant as before; indeed, there is little difference in the note on the two sides. Fremitus is almost as well felt on the right as on the left side. The lower border of the right lung moves 3 cm. on deep inspiration in the midaxillary line. The breath sounds, though distant, are better heard than on the previous examination. The whispered voice sounds have a distant bronchial quality. The deep inspiration following cough is accompanied by numerous fine moist rales heard over the whole front. Roentgenogram shows that the right lung is beginning to expand.

December 31. Patient now feels well and is anxious to return to work. He has taken his temperature regularly during the past month, and it has never been over 99°. His pulse has been around 90. He still has a little pain in the chest when he stoops over. Examination now shows the percussion note to be resonant over the right side, with a little impairment above and below the clavicle and in the upper interscapular area. Breath sounds are vesicular and distinctly heard over the whole side, although not as loud as on the left. A few coarse, moist rales are heard on deep inspiration. The lower border of the lung moves 6 cm. on deep inspiration in the midaxillary line. The point of maximum impulse is in the fifth interspace, 7.5 cm. from the median line. The roentgenogram shows that the lung has completely expanded. There is marked increase in the mediastinal shadows and of the radiating bands to both upper lobes, particularly to the right. Three sputum examinations have been negative for tubercle bacilli.

November 8, 1910. Patient returns to the dispensary saying that on November 4, after lifting a weight, he suddenly experienced pain in the left chest. Since then he has had some pain in the side, but he has practically no shortness of breath or other discomfort.

*Examination.* Patient looks comfortable; there is no dyspnea. Pulse and respirations not increased in rate. The left side of the chest is fuller than the right, although there is little movement seen on the left side. The note over the left chest is hyperresonant, but not markedly so. There is practically no cardiac dullness to the left of the sternum. Breath sounds on the left side are almost entirely absent. On the right they are loud and harsh. On the right the lower border of pulmonary resonance descends 6 cm. on full inspiration. On the left resonance extends to the same level as resonance on the right in full inspiration and this point does not change on inspiration and expiration. Litten's sign is well seen on the right; it is absent on the left. Roentgenogram shows a definite pneumothorax on the left side. The upper lobe is only partially collapsed; the lower lobe more markedly; there is moderate displacement of the heart to the right.

November 23. Patient has been feeling well, and has had practically no dyspnea. Percussion note is now resonant on both sides and the breath sounds heard with normal intensity over the left. The roentgenogram shows that the lung has completely expanded and that the heart has returned to its normal position.

December 10. Has felt perfectly well except that he caught a cold last week and has had some pain, generally distributed over the chest. At present he has considerable cough and a little morning expectoration. He thinks the expectoration comes mainly from the nose. A sputum examination has been negative.

*Examination.* Patient looks well; the lips and nose are a little blue, but the morning is cold. The right clavicle is a little more



prominent than the left, and the right shoulder droops a little. The left shoulder moves a little more freely than the right; the lower part of the right chest moves a little more freely than the left. The note is everywhere resonant, except there is a little impairment above and below the right clavicle and in the right supraspinous fossa. The lower border of the lung in the midaxillary line moves 6 cm. on the right and 5 cm. on the left on full inspiration. Fremitus is everywhere well felt, somewhat better on the right than on the left side. The breath sounds are everywhere loud and vesicular, rather harsh over the right upper lobe. The point of maximum impulse is in the fifth interspace just inside the mammillary line; there is a normal area of cardiac dullness.

December 27. Patient returns, stating that on the evening of December 24, while sitting quietly in a chair, he was taken suddenly with a sense of discomfort in the left side, which gradually increased in severity, particularly when he attempted to lie down. At present he has no pain except when he stoops over. On walking fast he has some pain in the left side and is a little short of breath, otherwise he has no dyspnea.

*Examination.* The patient looks well. The left side is more prominent than the right; it moves with respiration, but less than the right. The left chest is hyperresonant throughout. Fremitus is absent on the left side, and the breath sounds are absent except in the interscapular area, where they are very distant, and have a slight amphoric quality. The point of maximum impulse is seen just to the left of the lower end of the sternum. The roentgenogram shows a well-marked pneumothorax on the left side, with marked dislocation of the mediastinum to the right. The lung is generally although not completely collapsed.

January 14, 1911. Patient has been feeling quite well, although the cough has at times been troublesome. He has had very little shortness of breath except when he attempts to walk rapidly. He has no pain in the chest except on lying down. He has taken his temperature regularly during the past two months, and it has never been over 99°. Pulse ranges from 72 to 104, but is usually in the neighborhood of 80. Examination shows the movement to be good on both sides, only a little limited on the left. The note is a little hyperresonant over the whole left side, but nowhere tympanic. Breath sounds are still almost completely absent. Fremitus is felt, but diminished in intensity. The whispered voice sounds are very distant with a suggestion of metallic quality. The roentgenogram shows the pneumothorax has largely cleared up, although the lower lobe is not yet completely expanded.

February 4. Patient feels well. He has at times fleeting pains about the chest. The heart is now in its normal position and the signs of the pneumothorax have entirely disappeared. All over the left front and over the upper left back numerous fine superficial scratchy rales are heard on deep inspiration.

February 18. Patient is feeling exceptionally well and is anxious to return to work. The physical signs show, as they have on all previous examinations, a little impairment and harsh breathing over the right upper lobe. The cutaneous and conjunctival tuberculin tests repeated on January 30 showed absolutely no reaction.

November 21. Patient was well until one week ago, when he began to have pain over the right front of the chest. Pain came on after slipping and straining his chest. Since then the pain has persisted, and he comes thinking a pneumothorax has developed again. He has a little cough and the pain is aggravated on coughing. He has taken his temperature the last few days, and it has constantly been a little over 99°. Patient looks well, his color is good, and he is in good spirits. Examination shows no evidence of pneumothorax. The percussion note is a little impaired above and below the right clavicle and in the supraspinous fossa where breath sounds are harsh and shrill. Over both the lower front and back there are a few coarse moist and a few fine crackling rales.

March 29, 1913. Patient comes complaining that for the past three or four days he has had severe pain in the lower left chest. The pain is particularly severe when he lies down. Last night he was unable to sleep on account of it. He thinks he has had a recurrence of the pneumothorax.

*Examination.* The patient looks well; is a little blue, probably from the cold. Percussion note is everywhere resonant, except for slight impairment over the right upper lobe. The heart is in its normal position. The lower borders of both lungs move freely on inspiration. Over the left lower front there is a shower of fine moist rales on deep inspiration.

August 2. About ten days ago patient was suddenly taken with severe pain in right side of chest. The following day on stooping over the pain was so severe that he fainted. His family physician told him the pain was due to pleurisy, and says he found tubercle bacilli in the sputum.

*Examination.* The patient's general appearance is as it has always been, quite good. Besides the impairment which has been heretofore noted on the right side, there are numerous moist and a few sonorous and sibilant rales over the whole front and in the supraspinous fossa in back. The sputum contains numerous tubercle bacilli. Patient admitted to the State Sanatorium.

April 25, 1914. Patient was at the State Sanatorium from August 27, 1913, to April 12, 1914. He has improved somewhat in his general condition, and has less cough and expectoration. The physical examination now shows impairment on the right to the third rib and fifth dorsal spine with harsh, blowing breath sounds and fine moist rales over whole front and to the sixth dorsal spine in back. On the left there is a little impairment above and below the clavicle, and in the back down to the third dorsal spine

with roughened breath sounds and moist rales above and below the clavicle and in the supraspinous fossa.

While the case above detailed was under observation I had the opportunity of seeing another instance of pneumothorax coming on in a healthy young man without apparent cause which ran an almost symptomless course and subsided completely in a few weeks:

*CASE II.—Healthy young man has sudden pain in left side of chest followed by dyspnea on exertion; examination the following morning, November 30, 1910, reveals complete left pneumothorax; uneventful recovery in four weeks; has remained well since.*

White male, aged twenty-nine years, came to me for examination on November 30, 1910. There was nothing of importance in the family history. He had always been strong and healthy, except that since childhood he had had attacks of renal colic often associated with hematuria. Detailed examination had shown a large left hydronephrosis with almost complete absence of renal function on that side. On the evening of November 29, as he was leaving his house after dinner, he suddenly felt a sharp pain in the left side, followed by a sensation as though something had given way. He went to his office and again experienced the pain, especially on movement. He felt as though inspiration did not fill out the left lung; as he expressed it, "as though air went only half-way down the chest." However, he did not feel ill and had no shortness of breath. He attended a meeting of the Bar Association, after the meeting enjoyed a light collation, and then walked with a friend to his club, about two miles away, and sat there reading until midnight. On the morning of November 30, as he left home, he again experienced the curious sensation in the left side. He had an appointment on that morning to have Roentgen-ray pictures taken of his kidneys; he reported to Dr. Geraghty for this purpose, who postponed the investigation when he heard of the patient's symptoms, and sent him to me for examination.

Patient was a large, well-nourished man of good color and healthy appearance. Chest well formed and symmetrical. Inspection revealed at once a marked difference in movement on the two sides of the chest, the right moving freely, the left very little. Percussion note was resonant over both sides—a little hyperresonant over the left, though the difference between the two sides was not marked. The breath sounds were absent over the left side. On the right the lower border of the lung was at the eighth rib in the axillary line and the lower border moved 8 cm. on deep inspiration; on the left the lower border of resonance was at the tenth rib and did not move on deep inspiration. The point of maximum impulse was not definitely visible. There was very little cardiac dulness to the left of the sternum. The heart sounds were much louder on the right than on the left. Roentgen-ray examination showed a well-marked pneumothorax on the left side. The upper

lobe markedly collapsed; the lower lobe widely separated from the diaphragm, but adherent to the chest wall in the axillary area at about the fifth rib. The heart moderately displaced toward the right.

December 19. Patient spent a week in bed and then began going about. He has had absolutely no fever, and the pulse and respiration rate have been normal. He has felt perfectly well except for a feeling of uneasiness in the left side when he bends over.

*Examination.* There is still considerable diminution of movement on the left side. Fremitus is well felt on the left but not nearly so well as on the right side; the breath sounds are heard on deep inspiration, and are then vesicular in quality. Over the lower front and below the angle of the scapula behind there are numerous fine moist crackling rales on deep inspiration.

January 1. Roentgen-ray examination shows that the pneumothorax has completely cleared up. The mediastinal shadows are dense and broad shadows radiate from the mediastinum toward the periphery. The shadows are denser in the right upper lobe than elsewhere. The heart is in its normal position.

January 7. Patient feels quite well; he has taken his temperature continuously and has had no fever. Occasionally he has a stitch in the left side.

*Examination.* Movement is almost equal on the two sides, perhaps a little diminished on the left. The left clavicle is a little more prominent than the right. Percussion note is everywhere resonant and the breath sounds are loud and vesicular on the two sides. At the left base there are a few fine rales on deep inspiration. The *A. r. z.*—right, 6 cm.; left, 7 cm. The 1 per cent. conjunctival tuberculin test is negative; the cutaneous test gives a slight reaction.

January 1, 1915. Patient has been seen frequently since his recovery from the pneumothorax. He has remained well, has had absolutely no pulmonary symptoms, and the examination remains unchanged.

During the past year I have seen three more cases in many respects similar to the two described. Two of these are almost identical with Case II, while the other presents interesting points of difference.

CASE III.—Dispensary No. F. 9082.

*Healthy patrolman, aged thirty-eight years, has sudden pain on left side, followed by dyspnea on exertion; examination reveals left pneumothorax; uneventful recovery in four weeks; has remained well.*

White male, aged thirty-eight years, came to the Johns Hopkins Hospital Dispensary July 7, 1913, complaining of severe pain in the left side. The family history contains nothing of importance. The patient has always been a healthy man, and has had no serious illness since childhood. He is a patrolman and works at night. On the morning of July 4, patient reached home early in the morning

and went to bed. About noon, when he arose, he had severe pain in the left side of chest. However, in the evening he went to work as usual, but noticed on making his rounds that he was rather short of breath. Since then whenever he lies down or walks he has noticed the shortness of breath. During this time he has had pain in the left side.

*Examination.* Patient is a large, well-nourished man of healthy appearance. Mucous membranes are good color; no general glandular enlargement. Teeth are in bad condition and there is well-marked pyorrhea. Chest is well formed, though for a man of his build is rather long and narrow. The shoulders droop considerably, the left a little more than the right. The costal angle is about 80 degrees. The clavicles are equally prominent. Movement is markedly restricted throughout the left side. Percussion note over the right lung is normally resonant and the breath sounds are everywhere vesicular. There are a few fine moist rales over the lower front and in the lower axillary area. The lower border of the right lung is at the eighth rib in the axillary line and moves 6 cm. on deep inspiration. In the back the lower border of the lung is at the eleventh dorsal spine, and there is an excursion of 6 cm. between deep inspiration and full expiration. Over the whole left side of the chest the note is hyperresonant and rather drum-like in quality. The lower border of resonance is at the ninth rib in the axillary line. This point does not change with respiration. In the back the lower border of resonance is at a point between the twelfth dorsal and first lumbar spine and does not move with respiration. Fremitus is absent over the whole left side. Above the clavicle the breath sounds have a distant amphoric quality; elsewhere they are inaudible. The whispered voice sounds are scarcely audible over the upper portion of the chest, while in the axillary area and below the angle of the scapula they have a distinct, ringing, metallic quality. Cardiac pulsation is seen to the right and left of the sternum; cardiac dullness extends 5.5 cm. to the left and 6.5 cm. to the right of the median line. Heart sounds are clear, much louder on the right than on the left of the sternum. The pulse is slow, 76 to the minute, good size, regular. The vessel wall is palpable. Abdomen is normal in appearance; no rigidity; no tenderness. The liver is not felt; area of liver dullness is not enlarged. Spleen is not felt; area of splenic dullness is not enlarged.

July 19. Patient feels well. When lying down or walking he often has a sensation of rubbing over the left lower front. He walks about now with little discomfort. The percussion note is less hyperresonant on the left than it was at the first examination, and the breath sounds are audible over the left upper front. Cardiac dullness extends 8.5 cm. to the left and 4.2 cm. to the right of the median line.

August 2. Patient feels fairly well. He still has a little pain

in the chest, and at times he has shortness of breath when he walks rapidly. The percussion note is now almost equal on the two sides. Frenitus is still somewhat diminished in intensity on the left, but it is well felt everywhere. Breath sounds are audible over the left side, not so loud as on the right, and are accompanied by a profuse shower of fine moist rales over the lower front. Cardiac dullness extends 9 cm. to the left and 3.5 cm. to the right of the median line. There is a distant pleuropericardial friction rub to the left of the ensiform.

September 1, 1914. Patient has not returned for examination, but in reply to a letter states that he has remained perfectly well.

*CASE IV.—Young man, aged thirty-five years with relatively inactive chronic pulmonary tuberculosis, suddenly has severe pain in the left side. Examination reveals left pneumothorax. No constitutional symptoms develop and the pneumothorax heals uneventfully in five weeks.*

White male, aged thirty-five years, came for examination on October 1, 1912. There is a marked history of tuberculosis in the family. Patient has always been well but never robust, subject to frequent colds, some continuing rather obstinately. During the previous spring he had had grip, and his physician found evidence of tuberculous trouble in the chest.

*Examination.* Patient is a sparely nourished man of good color but looks below par in health. Pupils are equal and react actively to light; eye movements are all normal; no general glandular enlargement. Chest is long and thin, the right clavicle a little more prominent than the left, right shoulder sags a little and a little curvature of the spine to the right in the upper dorsal region; diminution of movement over the right upper. On the right the note is impaired above and below the clavicle and in the supraspinous fossa; breath sounds are a little blowing in quality, and after coughing there is a small number of fine moist rales to the third rib in front and to the fourth dorsal spine in back. On the left the percussion note is impaired to the second rib and in the supraspinous fossa; breath sounds are harsh and a little blowing; a medium number of fine moist rales to the second rib in front and to the fourth dorsal spine in back. Opposite the second and third dorsal spine the whispered voice sounds have a bronchial quality. Area of cardiac dullness is not enlarged; heart sounds are clear. Abdominal examination shows nothing noteworthy.

January 5, 1914. Patient has been well except for occasional attacks of abdominal pain which were diagnosed appendicitis and in July, 1913, the appendix was removed. Since the operation patient has been very well and has gained somewhat in weight. He never has cough and has not had any expectoration. Yesterday afternoon, after dinner, he had a sudden, sharp pain in the left lower axillary region associated with a feeling as though he wanted

to take a deep breath. He went home without any distress, but feeling chilled got into bed. After a few hours he felt perfectly well except that on deep breathing and movement there was some pain on the left side. During the night patient had some pain over the whole left side, radiating to the left shoulder.

*Examination.* Patient is lying comfortably in bed. He says he feels perfectly well, except there is a little pain in the left side when he turns over. Patient looks well and is in good spirits. Temperature 98.2°; pulse 78; respirations 18. The chest is symmetrical. The movement is markedly restricted on the left side. The percussion note at once attracts attention, being markedly hyperresonant throughout the left side. The lower border of resonance in the anterior axillary line is at the ninth rib; in the back at the twelfth dorsal spine, and these points do not move on deep inspiration. Fremitus is felt all over the left side, but is markedly diminished in intensity. Above and below the clavicle and in the supraspinous fossa breath sounds are plainly audible, distant, and blowing in quality. Over a small area in the second and third interspace in the anterior axillary line there is frank and loud tubular breathing; elsewhere over the chest breath sounds are inaudible. The whispered voice sounds are diminished in intensity everywhere over the side without change in quality. Over the small area in the second and third interspace where the breathing is tubular there is frank bronchophony. On the right percussion note is resonant except there is a little impairment above and below the clavicle and in the supraspinous fossa. The breath sounds are loud and vesicular in quality. After coughing there are moist rales to the second rib and to the fourth dorsal spine. The lower border of pulmonary resonance is at the seventh rib in the anterior axillary line, in back at the eleventh dorsal space; the border moves freely with respiration. Cardiac pulsation is seen to the right and to the left of the sternum. Cardiac dullness extends 5 cm. to the left and 6 cm. to the right of the median line. Heart sounds are louder to the right than to the left of the sternum.

January 20. After spending a few days in bed the patient got up and has been going about. During this time he has had absolutely no fever and the pulse and respiratory rate have been normal. He has a little shortness of breath on exertion and some dull pain over the left side. The percussion note over the left front has completely lost its hyperresonant quality, but hyperresonance persists over the left back below the angle of the scapula. Fremitus is still much diminished in intensity. Breath sounds are now audible over the upper front and the whispered voice sounds are better heard. The lower border of pulmonary resonance is at the eighth rib in the axillary line and there is an excursion of 4 cm. on deep inspiration. Heart dullness extends 10 cm. to the left and 4 cm. to the right of the median line.

February 21. Patient now feels perfectly well except that at times he has a little twinge of pain on the left side. Examination shows that the pneumothorax has completely disappeared and the conditions are the same as they were on examination before the onset of the pneumothorax. On the right the note is impaired to the second rib and to the third dorsal spine and there are rales after coughing to the second rib and to the fourth dorsal spine. On the left the note is impaired to the second rib and to the fourth dorsal spine, and moist rales are heard after coughing to the third rib and in back down to the angle of the scapula.

December 12. Patient has been quite well; he has gained a little in weight; he never has cough or sputum; indeed, feels that he is in very good health and the pulmonary examination shows the same conditions as on February 21.

*CASE V.*—A healthy man, aged twenty-nine years, suddenly has severe pain in the right side on the morning of July 29, 1914, followed by a little dyspnea on exertion. Examination on August 17, 1914, reveals a right-sided pneumothorax which has almost completely cleared up. Patient has remained well since then.

H. T., white male, aged twenty-nine years, came for examination on August 17, 1914. There is nothing of importance in the family history. The patient, though never robust, has always been healthy. Whooping cough, measles, and scarlet fever in childhood; no serious illness since. On the morning of July 29, the patient took an early train and went into the diner and ordered breakfast. He was feeling in his usual good health. While sitting at the table he suddenly had a catch in his right side, which bent him over and immediately after he had a feeling of oppression and some difficulty in getting his breath. The pain in the side was increased whenever he took a deep breath. Following this the patient had a little cough and a little expectoration. The sputum has been examined a number of times and tubercle bacilli have not been found. His temperature has been taken frequently and occasionally has been a little above normal. The pain in the right side has almost completely disappeared although he still complains of a little soreness. During the past week he has had no shortness of breath on ordinary exertion.

*Examination.* Temperature, 98°; pulse, 80; respirations, 20; weight 144½ pounds; height, 5 feet 9 inches. Patient is a sparsely nourished man. His complexion is a little sallow; mucous membranes are good color. Pupils are equal and react actively to light. Eye movements are all perfectly normal. Teeth are in good condition, there is considerable dentistry; no pyorrhea. The throat is a little injected; there is no gross abnormality. Posterior cervical glands are all easily palpable but not markedly enlarged; the glands below the angle of the jaw on both sides are a little enlarged; the epitrochlear glands are just felt; the axillary glands are easily felt.



The chest is long and rather thin; the costal angle is about 80 degrees; the right shoulder is considerably lower than the left and the right clavicle a little more prominent. Movement is diminished over the right side. The spine is straight. Percussion note over the right front is a little hyperresonant in quality. On the left it is normally resonant, the difference between the two sides being by no means marked. The lower border of resonance is at the ninth rib on the right side; at the eighth rib on the left in the midaxillary line. On the left side the lower border of resonance shows a movement of 5 cm. on deep inspiration, whereas on the right there is none, or at most not more than 1 cm. of movement. Fremitus is well felt over the right side, but it is diminished as compared with the left. On quiet breathing breath sounds are entirely absent over the right side; on deep breathing they are very faint and distantly tubular in quality. The whispered voice sounds are diminished in intensity, but have a distant bronchial quality, and just below the clavicle they have a slight metallic quality. On the left breathing is everywhere loud and vesicular; no rales are heard. Heart: The point of maximum impulse is in the sixth interspace just inside the nipple line. Cardiac dullness extends 11 cm. to the left of the median line; there is no cardiac dullness to the right. The heart sounds are perfectly clear. They are absent to the right of the sternum. Abdomen is normal in appearance; abdominal wall is soft and relaxed. Liver is not felt; liver dullness does not extend below the costal margin. Spleen is not felt; area of splenic dullness is not enlarged. The right kidney is just palpable; the left is not felt. Pulse is regular, good volume and good size; the vessel wall is not thickened. Blood-pressure: systolic, 120; diastolic, 70. Roentgen-ray examination shows pneumothorax of the right side. However, the lung has expanded so that at some points it has almost reached the chest wall. Marked increased density of the mediastinal shadows and of the shadows generally throughout the lung. There is slight clouding and flattening of the left apex.

November 1, 1914. The patient has not been seen again, but reports that he has remained perfectly well.

DISCUSSION. These five cases are of interest, since they illustrate (1) how insidious may be the onset of pneumothorax; (2) what few symptoms it may occasion; (3) how easily upon a casual examination the condition may be overlooked; (4) the perfectly benign course of the affection; (5) the occurrence of an insidious benign type of pneumothorax in perfectly healthy individuals as well as in those with manifest pulmonary disease.

This benign type of pneumothorax coming on without apparent cause and subsiding uneventfully has received a fair share of literary attention. The condition has been frequently described in England, less commonly in France, only occasionally in Germany, and though there are a few good accounts of it in American literature,

still it has not attracted wide consideration. Fussell and Riesman<sup>15</sup> reviewed the literature of spontaneous pneumothorax in 1902 and analyzed 56 cases. Nikolsky,<sup>29</sup> in 1912, collected 90 cases from the literature. Some authors emphasizing the obscure cause of the pleural rupture have termed the condition "spontaneous pneumothorax" (Nikolsky;<sup>29</sup> Emerson,<sup>11</sup> Bach,<sup>3</sup> Hamilton<sup>20</sup>); "idiopathic pneumothorax" (Boland,<sup>7</sup> Francine and Landis<sup>14</sup>), and "pneumothorax in the apparently healthy" (Weber,<sup>37</sup> Hall,<sup>19</sup> Male<sup>27</sup>), to distinguish it from pneumothorax following violence or gross pulmonary disease. Others, struck by the absence of the usual symptoms accompanying pneumothorax, have described it as "latent pneumothorax" (Bevan,<sup>5</sup> Stevens<sup>36</sup>), "pneumothorax with insidious onset" (Pepper<sup>30</sup>). Still others, having missed certain classical physical signs of pneumothorax, have called it "pneumothorax muet" (Yaldizdjian<sup>41</sup>) and "pneumothorax silencieux" (Adler<sup>2</sup>). Finally, many have emphasized certain salient features, using such descriptive terms as "recurring pneumothorax" (Finny,<sup>12</sup> Gabb,<sup>16</sup> Sale<sup>35</sup>), "pneumothorax with rapid recovery" (Coghlan,<sup>10</sup> Beevor<sup>4</sup>), "spontaneous, non-tuberculous pneumothorax" (Fussell and Riesman<sup>15</sup>), "curious instance of pneumothorax" (Jochmann<sup>22</sup>), etc.

None of the terms that have been suggested for this type of pneumothorax are satisfactory, but "spontaneous pneumothorax" is the term most commonly employed; and though it describes only one of the many important features of the condition, still it is the least objectionable, if we will accept its extension to embrace them all. In this sense spontaneous pneumothorax signifies a pneumothorax coming on in apparently healthy individuals without ascribable cause; resulting in no infection of the pleura and therefore unaccompanied by constitutional symptoms; and healing rapidly and completely in a few weeks.

As regards the meaning of "apparently healthy," I may say that most authors would exclude from the group of spontaneous pneumothorax those cases in which examination before or after the occurrence reveals definite pulmonary disease. The "non-tuberculous" nature of the condition is constantly emphasized. I feel very strongly that no such sharp line can be drawn, and I would include tuberculous cases that meet the other requirements of the definition. Case I certainly belongs to the group of spontaneous pneumothorax, and still years later he developed a manifest pulmonary tuberculosis. Both immediately before and immediately after the attacks of pneumothorax the clinical evidence was not sufficient to make a diagnosis of pulmonary tuberculosis, although in the light of later developments it seems certain that even at that time he must have had the infection. Cases II, III, and V in no way distinguishable from Case I have remained well. Case IV, though in good general condition, still had a definite pulmonary

tuberculous lesion before the onset of the pneumothorax. In all other respects the clinical picture was identical with that of the three previous cases. The absence of grave pulmonary disease, of pleural infection, and of mechanical conditions leading to high intrapleural pressure distinguish the condition from pneumothorax as it usually occurs in pulmonary tuberculosis. Later I will speak of the mechanism of the production of the pneumothorax in spontaneous pneumothorax and here wish only to remark that in all probability the mechanism in Case IV was the same as in the previous cases, and was not due, as pneumothorax in advanced pulmonary tuberculosis usually is, to the rupture of the pleura by a tuberculous focus.

While most cases of spontaneous pneumothorax remain simple, in a small number pleural effusion develops. Cases in which the effusion is the expression of an infection must be discarded from the group, but in a certain number the fluid remains sterile, no constitutional symptoms develop, and the fluid and air are both rapidly absorbed. Such instances are reported by Francine and Landis,<sup>14</sup> Hamilton<sup>20</sup> and West.<sup>33</sup> In some instances the fluid is bloody, apparently due to hemorrhage at the time of the pleural rupture. Rolleston's case<sup>34</sup> proved fatal and no cause for the pneumothorax or hemorrhage could be found at autopsy. Pitt's patient,<sup>31</sup> a lad, aged eighteen years, died within thirty-six hours of the onset of pain in the side. At autopsy a ruptured emphysematous bulla was found with a torn adhesion attached near it. Boland's patient<sup>7</sup> recovered after aspiration of thirty-four and then thirty-nine ounces of blood. Ness and Allen's patient<sup>25</sup> recovered uneventfully; apparently the hemorrhage was very small.

As regards the third characteristic in the definition, rapid and complete healing, one can set no absolute limit. In most cases the pneumothorax disappears in from four to eight weeks. Occasionally the pneumothorax will persist longer than eight weeks and then clear up completely, but a duration of over eight weeks is against including the case in the group of spontaneous pneumothorax.

The changes in the lung that occasion the pleural rupture are not clinically ascertainable, but there are enough autopsies on record to make clear the mechanism in many instances. Zahn,<sup>42</sup> in 1891, published the first thorough study of "pleural rupture without inflammation," and described four different modes:

First, the rupture of vesicular blebs. In one case he reports there were a number of such bulke in the region of the apex of the left lung, and upon inflating the lung one of these showed a small rent. In another instance associated with well-marked pulmonary emphysema, numerous bullae were found on the surface of the right lung, some as large as a hen's egg; one of these showed a tear 2 mm. in length. Zahn collects from the literature similar observations by Duvilliers, Dittrich, Fraentzel, and Rheder. Rankin,<sup>32</sup>

and Cnopf<sup>9</sup> may be added to the list. Bach<sup>3</sup> collects fifteen cases from the literature.

Second, the rupture of interstitial emphysema blebs. In these cases air enters the interstitial tissue, then reaches the pleural surface, where a vesicle is formed, which then ruptures. All such instances of interstitial emphysema have been about pleural adhesions, and the pleural adhesions are the primary condition which give the mechanical explanation for the interstitial emphysema. Zahn<sup>12</sup> reports two instances of pneumothorax produced by this mechanism. In both instances there was associated pulmonary tuberculosis, but the pleural rupture was about adhesions and not contiguous to tuberculous foci. He considers this the most common cause of rupture in spontaneous pneumothorax.

Third, a direct tear of the pleura by the tug of adhesions. Zahn<sup>12</sup> reports such a case in a suicide, and thinks the instance reported by Robertson belongs to this group.

Fourth, senile atrophy of the pleura. A man, aged sixty-one years, with extreme emphysema, showed at autopsy a number of minute openings in the pleural surface over an area where the membrane was extremely thin. Zahn remarks that he had never before seen such an extreme grade of emphysema, and he regarded the pleural atrophy to be due to pressure. I have encountered no similar observation in the literature.

We may exclude division four, since it is an unusual cause of pneumothorax, and it is a technical refinement to separate divisions two and three. Such postmortem evidence as is available, therefore, points to the rupture of vesicular emphysematous blebs and the tears produced by adhesions as the two common causes of spontaneous pneumothorax. The not infrequent finding of ruptured vesicular blebs has led some authors, for instance Bach,<sup>3</sup> to speak of the whole group under consideration as "spontaneous pneumothorax in emphysema." Anyone who has had a large experience with pulmonary cases will remark at once how surprisingly infrequent pneumothorax is in the frankly emphysematous. It is noteworthy that spontaneous pneumothorax is a disease of early adult life, over 80 per cent. of the instances collected by Nikolsky occurring before the age of forty years. Therefore, it is manifestly improper to regard spontaneous pneumothorax as having any direct relation to general pulmonary emphysema. When emphysema is its cause the emphysema is generally a local condition, and clinical evidence is, in my opinion, strongly in favor of adhesions being the usual condition underlying the pleural rupture.

Having in mind the mechanism of spontaneous pneumothorax, it will appear unreasonable to exclude from the group cases with pulmonary tuberculosis in which the onset and benign course of the pneumothorax and the rapid recovery are the characteristic features (such cases are reported by Coghlan,<sup>10</sup> Knight,<sup>23</sup>

Hamilton<sup>20</sup>). There is considerable evidence to influence us to believe that tuberculosis is the commonest cause of pleural adhesions, and if this be true it is further reason against drawing too close a line between manifest and obscure pulmonary tuberculosis, a distinction that at once involves serious clinical difficulties. Of course, it is possible that an isolated tubercle situated upon the pleura might rupture and the opening be so small that it would heal promptly without the pleura becoming infected. Such an occurrence, however, must be very uncommon. Letulle reports a diabetic without evidence of pulmonary disease who developed pneumothorax. Eight days later he died suddenly and autopsy revealed a single tuberculous nodule in the lung which had ruptured. West<sup>33</sup> and Flint<sup>13</sup> report instances of pneumothorax due to the rupture of a single small tuberculous cavity. However, neither of the cases resembled clinically spontaneous pneumothorax, for West's patient died shortly after the onset of pneumothorax from exhaustion, and although Flint's patient died of pneumonia, the hydropneumothorax had persisted for a long time before.

The clinical symptoms in spontaneous pneumothorax indicate that in most instances the pleural opening is very small. Symptoms of high intrapleural pressure are seldom present, and in the two cases I followed carefully with Roentgen-ray examinations the lung was not fully collapsed. Apparently as soon as sufficient air escapes into the pleural cavity to cause an appreciable decrease in the intrapulmonary pressure the pleura is relaxed and the opening closes. The size of the opening will determine the degree of pulmonary collapse.

In the definition of spontaneous pneumothorax the salient clinical features were emphasized. Briefly, the important points are these: The condition predominates in males: 45 males to 10 females in Fussell and Riesman's<sup>15</sup> series and 73 males to 14 females in Nikolsky's<sup>29</sup> group. The vast majority of the cases occur in young adults. In Nikolsky's table two instances are under fifteen years of age, 34 between fifteen and twenty-five years, 26 between twenty-five and forty years, 11 over forty years. The right and left side are affected with equal frequency. The exciting cause in many instances is exertion, though the exertion may be slight and entirely out of proportion to the result. Not infrequently the pneumothorax comes on without any provoking cause, and in some of the reported instances it developed during sleep (Fussell and Riesman,<sup>15</sup> Landmann,<sup>24</sup> Heitler,<sup>21</sup> Sale,<sup>35</sup> Bevan<sup>5</sup>). Nikolsky's analysis shows that an equal number follows exertion and comes on without exertion. The insidious onset is emphasized particularly by Pepper<sup>20</sup> and Jochmann.<sup>22</sup>

The symptoms at onset vary from extreme dyspnea and collapse to disturbances so slight as scarcely to attract attention. In the instances reported in this paper, pneumothorax would not be

suspected from the symptoms. Nearly always there is some dyspnea on exertion, but there is seldom distress when the patient is at rest. The mild character of the symptoms is a peculiar and characteristic feature of the condition. No doubt the size of the rupture largely determines the intensity of the symptoms. Cough is often present, but frequently is entirely absent, and is seldom troublesome. A characteristic feature of the condition is the absence of constitutional symptoms, of fever, and of other evidence of infection.

The duration of the pneumothorax varies. In most instances there is complete restitution in six weeks. Of 66 cases collected by Niklosky,<sup>29</sup> 59 recovered completely within two months; 6 during the third month; 3 during the fourth month. There are certain curious instances of pneumothorax that have persisted for a long time. Bittorf<sup>6</sup> reports a case which under his observation remained unaltered for a year and a half, and from the history he concluded that the pneumothorax had probably been present for twenty-five years. Whitney<sup>39</sup> thinks in his patient the pneumothorax had arisen seven years before his examination. Adams' patient recovered after the pneumothorax had persisted for five years.

I have found in the literature sixteen instances of recurrence of the pneumothorax (Jochmann,<sup>22</sup> Hall,<sup>19</sup> Bull,<sup>8</sup> Goodhart,<sup>17</sup> Gabb,<sup>16</sup> Sale,<sup>35</sup> Finney,<sup>12</sup> West,<sup>38</sup> Flint,<sup>13</sup> Knight,<sup>23</sup> Weber,<sup>37</sup> Rendu,<sup>33</sup> Maillart and Lasserre,<sup>26</sup> Wieruzski,<sup>40</sup> Grenier,<sup>15</sup> Bach<sup>3</sup>). Gabb's patient had four attacks all on the same side. Sale's patient apparently had eleven attacks during six years. In many of the cases the recurrence was, properly speaking, a relapse, the second attack of pneumothorax coming so promptly upon the resolution of the first as to warrant the inference that the original tear had reopened. Three of the cases are of particular interest, since, as in Case I of this report, the recurrence occurred on the opposite side. Goodhart's patient, a young man, aged twenty-four years, had a pneumothorax of insidious onset on the right side in May, 1891, another coming on in like manner in July, 1892, but on this occasion affecting the left side. He recovered from both attacks uneventfully, and was well three years, after. Wieruzski reports about a physician, aged fifty-four years, who had had bronchitis and emphysema for a long time. In the fall of 1894 he had pneumothorax on the right side that cleared up completely in about five weeks, but recurred a few weeks later. In February, 1899, he again developed pneumothorax, this attack being on the left side, which likewise cleared up in a few weeks. In September, 1899, he had another attack on the right side. Grenier gives the account of a young man, aged twenty-one years, who had a spontaneous pneumothorax on the left side in the fall of 1903. In December, 1904, he had an identical attack involving the right side, and in March, 1905, a

recurrence upon the right side. Recovery from all three attacks was rapid and uneventful.

After an attack of spontaneous pneumothorax the individual may remain well indefinitely. One of Hamilton's patients was well after ten years; another after six years; Fussell and Riesman's case after seven years; Bach's three years; West's ten years. A characteristic case of spontaneous pneumothorax was in the Johns Hopkins Hospital in January, 1898.\* The patient returned to the hospital in November, 1913, complaining of digestive disturbances and jaundice. During the interval he had been well and had had no pulmonary symptoms. The pulmonary examination on the second admission showed no abnormality other than a few crackling rales at the left base.

As regards the examination it is important to emphasize that in these cases the physical signs of pneumothorax stand out in classical purity. Pneumothorax is so frequently accompanied by effusion and associated with gross disease of the lungs that there is a general tendency to emphasize accessory physical signs, namely, succussion, the coin sound, metallic tinkling, and movable flatness, rather than the fundamental signs peculiar to and characteristic of the condition. Laennec's description has been weakened by unessential additions. On inspection the affected side is not strikingly prominent, but there is always diminished mobility. Fremitus may be absent, but it is usually well felt, though greatly decreased as compared with the opposite side. The percussion note may be but little altered, and the change escape notice if the examination be hurried. On careful percussion the note is discovered to be hyperresonant, sometimes with tympanitic overtones. The striking feature on auscultation is the absence or great diminution in the intensity of the breath sounds. The voice sounds are less strikingly suppressed, and at times have a curious, characteristic metallic echo.

I wish to call attention particularly to the diagnostic value of percussion. Percussion of the lower lung border reveals that resonance stops on the affected side at the level reached by the lung on the sound side in full inspiration. This point is stationary, showing no variation with inspiration and expiration. The extension of pulmonary resonance to the full capacity of the pleural space with absence of respiratory variations at the border is absolutely characteristic of pneumothorax without effusion. If the note is hyperresonant the hyperresonance extends in front to the opposite border of the sternum. The heart is always displaced, and its position can be determined satisfactorily only by percussion.

The diagnosis is easily made if one thinks of pneumothorax, but in the entire absence of symptoms the condition may not be

\* Reported by Osler, Maryland Med. Jour., 1898, xxxviii, 461; Case 28 in Emerson's report.

suspected and the physical signs be overlooked. Case I at first attracted attention as an instance of unusually feeble breath sounds, without any satisfactory explanation for the enfeeblement. A physician experienced in the study of pulmonary disease saw this patient, and was sure he would have missed the diagnosis had the condition not been pointed out. Case III was first seen by an experienced instructor in physical diagnosis, who diagnosed a mediastinal tumor pressing upon the bronchus.

The treatment for the condition is to do nothing. The pulmonary collapse closes the pleural opening, the air in the pleural cavity is gradually absorbed, and as the lung begins to reëxpand the pleural rupture is tightly healed. Occasionally the pneumothorax recurs shortly after the lung has completely expanded, no doubt due to incomplete healing of the pleural wound.

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## THE OCCURRENCE OF ARTERITIS IN MENINGITIS.

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THE part played by inflammation in alterations of the intima of arteries is still an unsettled question. This is illustrated by the wide diversity of opinion which prevails among many of the foremost investigators. Some (Adami, Thoma, Jores) are of the opinion that the cases of chronic thickening of the intima are usually dependent upon mechanical disturbances, while others (Klotz, Hansen, Simnitsky) have shown that similar intimal changes may be found in the arteries of young individuals who had suffered from acute infectious diseases. The adherents of the mechanical theory hold that the intimal thickenings are commonly secondary to a medial weakening.

Rokitansky, an early investigator of nodular thickenings of the intima, held that they were the result of an organization of materials deposited from the blood stream upon the intimal surface of the

vessel. He was of the opinion that the intima, being a non-vascular structure, was not capable of undergoing an inflammatory change. The error of this view was clearly shown by Virchow, who described "endarteritis chronica deformans" as a parenchymatous inflammation of the intima, with active proliferation of the cellular elements and at the same time a metamorphosis of the intercellular substance.

Klotz has pointed out that the nodular aorta is the result of repeated insults telling upon the intima alone, and that the thickenings may be entirely proliferative, representing a chronic inflammatory production. Concerning the nodular thickenings about the intercostal arteries, he finds the reaction an inflammatory one and accompanied by progressive as well as degenerative changes in the tissues of the intima.

Again, we find that an endarteritis has been induced experimentally by the employment of various microorganisms. Klotz, who injected rabbits intravenously with *B. typhi* and streptococci of low virulence, obtained warty thickenings of the first part of the pulmonary and ascending limb of the aorta. Microscopically, these areas showed a fatty degeneration of the subendothelial tissue, with much connective tissue advancing into the degenerated area. Saltykow has noted similar results by the intravenous injection of staphylococci.

Boinet and Romary by the employment of different organisms (*B. typhi*, *B. coli*, streptococci, staphylococci, *B. anthrax*, tubercle bacillus, tetanus, and diphtheria) observed that tiny yellow plaques were produced in the aorta. Microscopically, there was a cellular infiltration in the intima, at times extending into the remaining layers, but most frequently almost entirely isolated to the adventitia around the vasa vasorum. Pernice studied the effect of the *Staphylococcus aureus* and found an inflammatory reaction in all three coats, consisting mostly of a round-celled infiltration, and in the most severe cases the inner layers of the intima contained large cellular elements.

Sumikawa, who irritated the vessels by painting them with turpentine or silver nitrate or again infected them with bacteria, demonstrated that the vessels so treated showed an inflammatory reaction in all the coats or else in the intima alone. It has been shown by Stumpf that in cases of infection by direct continuity the process proceeds from the adventitia inward and may advance to the intima, which may in turn develop a verrucose endarteritis.

Thus we find that not only is there a true endarteritic thickening of inflammatory origin, but also that the intima is capable of showing a definite inflammatory reaction with the presence of a cellular infiltration. However, the mode by which this reaction takes place, the relation of this inflammation to the different structures within the coats, is still open to discussion.

Koester believed that the primary lesion of arteriosclerosis was

an inflammation of the media. There is, he said, a chronic inflammation following the vasa vasorum from the adventitia into the media while the intimal reaction is only secondary to this. He further found that each plaque of endarteritis had one or more complementary areas of mesarteritis beneath it. In regard to the above discussion by Koester, we find the following noted in the recent work of Klotz. "The simultaneous presence of a small-celled infiltration in the vicinity of the vasa vasorum and the intima may be observed during the acute stages, but we have not been able to demonstrate a constant relation between them in the arterial wall. The localization of one or other in the artery is not always accompanied by a similar reaction in the other arterial coat opposite to it. In other words, though an inflammatory reaction may be demonstrated about the vasa vasorum in the adventitia and outer portion of the media a similar process may not be opposite to this in the intima. Moreover, where the simultaneous presence of a cellular infiltration has been observed in the inner and outer coats of the artery there has always appeared a strip of media adjacent to the intima which was uninvolved in the inflammatory process. It would, therefore, appear that these reactions are individual, though frequently occurring side-by-side in the same vessel. The cellular exudate found in the intima appears to arise by a direct migration of the wandering cells from the surface of the artery."

Although inflammatory diseases of the intima have long been recognized, we, nevertheless, feel that the exact character of the lesion is not generally recognized. It was not until recently that there has been specific information concerning this subject, and we would like very much to add supporting evidence to a process already so accurately described by Klotz.

In a previous study upon the reactions of elastic tissue to inflammation we have briefly made mention of the reaction seen in the vessel walls in a case of acute septic meningitis. Following this work we thought it of special interest to study the changes in the arteries of the meninges in the various types of acute meningitis. For this purpose we have selected cases of acute septic, tuberculous, syphilitic, and anthrax meningitis, together with blastomycosis of the meninges and acute anterior poliomyelitis.

The stage of the disease at which the patients died of acute septic meningitis always gave evidence of a simultaneous involvement of the meningeal arteries. At the beginning the intima was found very edematous and the cells widely separated, with a considerable pinkish staining granular debris between them. Whether this can be accurately taken as the initial stage in all cases is difficult to say. However, shortly following upon this edema there was seen a migration of inflammatory cells from the lumen of the vessel into the intimal tissues. Quite often inflammatory cells could be seen passing between the cells of the intimal endothelium, and it appeared as

though the endothelial cells were indented or plastic at these points of entrance. The endothelial covering of the intima could be made out in the majority of places and consequently allowed accurate study of the process. With the migration of these cells into the intima the latter became much thicker and more swollen, so that it formed a prominent, puffy inner layer (Fig. 1.) The cells which took part in this reaction consisted for the most part of polynuclear leukocytes, which extended through the entire depth of the intima to the internal elastic lamina. However, associated with the polynuclear leukocytes there were a fair number of lymphocytes and large phagocytic endothelial cells. In some specimens these endothelial cells appeared in great numbers, simulating not a little the grouping of endothelial cells in the more chronic lesions. Furthermore, amid the collections of endothelial cells were seen other cells like fibroblasts arising from the fixed cells of the intima and having elongated oval nuclei and swollen spindle-shaped bodies of clear

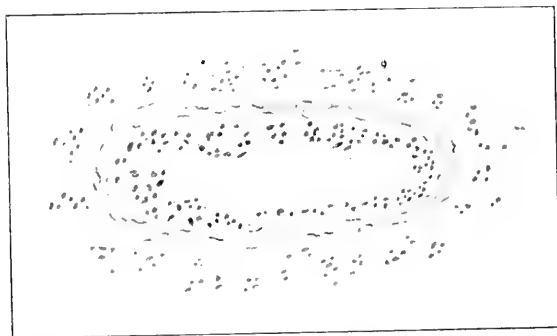


FIG. 1.—Septic meningitis. Acute inflammatory infiltration of intima.

cytoplasm. These cells appeared in the deep intima, but were also seen in the intermediate zone of this layer. The endothelial cells were large and round, with pale-staining protoplasm and centrally placed stippled nuclei. These cells were phagocytic for polynuclear leukocytes, lymphocytes, and a dark brown pigment.

In the intima of some of the vessels the pigment in the endothelial cells was not observed, while in others a fair amount of pigment, debris, and cells was found. The endothelial cells were often so crowded with phagocytosed cells and material that it was difficult to make out the nucleus proper. In some instances a number of red-blood cells were also seen in the lesion of the intima. In most of the vessels studied the internal elastic lamina formed the outer boundary of the inflammatory infiltration of the intima. It would appear that the inner elastic membrane is a very resistant layer and limits the extent of the inflammation for a relatively long time, although ultimately the barrier is overcome.

The adventitia is commonly invaded by the exudate which covers the meninges. This exudate is made up of large numbers of polynuclear leukocytes with lymphocytes and a considerable number of endothelial phagocytes. These cells invade the adventitia, but curiously enough stop at the outer border of the media. The striking feature of this is that in the same artery the infiltration of the intima has stopped at the inner elastic membrane, so that the media is left intact. In vessels so affected the media at this time shows no deviation from the normal. It would be well to note that in these vessels there is no demonstrable relationship between the reaction in the adventitia and that in the intima, and hence that the media cannot be the site from which the extension into the intima occurs. Another noteworthy feature is that the adventitia is quite often comparatively free from inflammatory cells while the intima is densely infiltrated, the entire circumference being uniformly affected.

Although the media is uninvolved in the earlier stages, it, nevertheless, becomes involved later on. This takes place by the cells advancing along the lymphatics from the adventitia and to some extent from the intima. The extension from the intima takes place only in a very small part after the inner elastic membrane has been injured by the inflammatory reaction in the intima. The weakening of the elastic layer is demonstrated by a Weigert elastic stain, which shows splitting and granulation of the fibers with inflammatory cells lying between the elastic threads. The fine split threads of elastic tissue bend into the intima, and in many places they can be seen lying among the inflammatory cells close to the parent layer. Notching and granulation of the inner border of the elastic membrane was a very prominent feature in these sections.

When (Fig. 2) the inflammatory reaction involves the media it is more intense in the outer layers of this coat. From this appearance it would seem that the inflammatory reaction in the media comes for the most part by the extension from the adventitia and advances to the outer border of the inner elastic membrane but rarely goes further. When an inflammatory infiltration was observed in the media the invading cells were sparsely scattered and rarely included all of the types seen in the intima.

The intima of the arteries of the blastomycotic and anthrax meningitis showed extensive infiltration by inflammatory cells, polymorphonuclear leukocytes, together with a fair number of large swollen endothelial cells being the principal types of the exudate. The reaction in the intima was particularly acute. An occasional leukocyte with acid-staining granules was seen. Although the reaction was most marked in the intima, there were a considerable number of inflammatory cells in the media and adventitia. These cells were confined to the coat in which they were found, and the internal elastic lamina seemed to act as a limiting membrane.

We found it took a fair time for the inflammatory products to bring about a sufficient change of the elastic layer to permit diffuse cellular migration, in which the intimal and medial reactions commingle and appear as if they had been part of a single process advancing from without inward. The change noted in these vessels conformed to the more advanced reaction observed in the arteries of acute septic meningitis.

In the arteries of tuberculous meningitis the vessel wall was only mildly involved, compared to the types previously described. The intima was moderately swollen, with the presence of occasional lymphocytes and polymorphonuclear leukocytes. The involvement never reached the proportions seen in the more acute infections. Inflammatory cells were seen scattered in the muscular wall, but the reaction was more particularly perivascular in character. This periarterial inflammation with lymphocytes was also the type observed in the syphilitic meningitis and anterior poliomyelitis.

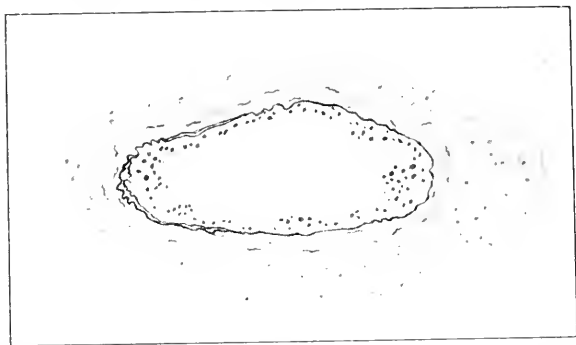


FIG. 2.—Septic meningitis. Splitting of elastic lamina through inflammatory process.

Sections of the acute septic meningitis stained with Sudan III, and hematoxylin showed the presence of fat in the cells contained within the intima. This fat was found in the form of fine granules, some of which were almost globular. It was present in the leukocytes and endothelial cells of the inflammatory infiltration. At times a slight fatty change was noted in the deep intimal tissue bordering on the elastic layer. The fat here appeared smooth and homogeneous. This was only slight in amount, and was not the rule, most of the fat being intracellular.

The presence of large endothelial cells in the intima of arteries have been described by Klotz and Anitschkow. Anitschkow fed rabbits with cholesterol mixtures and demonstrated doubly refractile lipoid bodies within endothelial cells in the intima of their arteries. Klotz noted that "similar cells may be commonly demonstrated in human arteries where the fatty degeneration occurs in the superficial layers of the intima, and when such specimens are cut (frozen)

on the flat they are seen as compact aggregations in which the lipoid substance is almost entirely intracellular." As previously mentioned we found endothelial cells in the intima containing fatty granules and small globules as well as other endothelial cells containing phagocytosed cells, fat, and blood pigment. We would draw particular attention to the phagocytic character of the endothelial cells observed in our specimens, and to note that it is not at all unlikely that the endothelial-like cells noted by other observers are of the same type.

It is almost impossible to definitely indicate the final results which occur in the arteries that we have examined, as these particular diseases are so uniformly fatal. However, there are several points to bear in mind which direct our attention toward the probable outcome of the arterial lesion. We have seen that the inflammatory process in the intima is accompanied by progressive as well as degenerative changes. Fibroblasts, several layers deep, were found proliferating in the swollen intima, and fatty substances were present in the superficial infiltrating cells and only rarely in the region of the internal elastic lamina. Most of the lipoid substances were intracellular, and much of it would, in all probability, have been removed by active metabolism in the stage of healing. In the end the fibroblastic proliferation would have brought about repair of the injured layer, leaving the intima thickened and hyalin in appearance.

Virchow demonstrated that the intima, like other non-vascular structures, may be the seat of inflammation, and that a proliferation of its own cells leads to the nodular masses on the surface. Moreover, the endarteritic thickenings of the aorta about the intercostal arteries have been recently proved by Klotz to be of inflammatory origin. He found the reaction an inflammatory one, accompanied by progressive as well as degenerative changes in the tissues of the intima and repair accomplished by a proliferation of the connective tissues of the inner layer of the intima. It was further noted by him that inflammatory reactions of the intima of longer duration are always accompanied by a connective-tissue disturbance of a proliferative kind, and from them there develop the intimal thickenings of the "hyalin" type.

There is still another process which must not be passed unnoticed, the great tendency for thrombosis in these vessels. With the marked involvement of the intima and at times disorganization of this layer we have a factor enhancing the coagulation of blood. Added to this the narrowing of the vessel lumen, slowing of the blood stream at irregular points, and an abnormal reaction of the inflamed tissue still further assists in producing thrombosis. In many of the vessels of acute septic infection there is total destruction of the intima, with early thrombosis. Fibrin and inflammatory cells are found in the deep intimal tissues and take a position between the

split fibers of the internal elastic lamina. The repair of such a process would eventually lead to obliteration of the arterial lumen. This alteration in the structure of the vessel has been variously indicated as "endarteritis obliterans" (Friedländer), "endarteritis productiva" (Orth), "thromboangiitis obliterans" (Buerger), and a type similar to the last described by Winiwarter.

In our discussion we wish to be clearly understood that our observations have been limited entirely to the study of acute cases. Further, although we have studied a variety of affections of the meninges, our opinion as to the ultimate outcome of the changes found is based for the most part upon the reactions occurring in the arteries of septic meningitis during the acute stage. The organisms associated with this affection are the most common factors in the production of acute purulent lesions in the body. They are commonly associated with septicemia, pyemia, and ordinary infections, to which we are all subject. Our findings are, therefore, very suggestive that if the opportunity is taken to study the systemic vessels in the various stages of infectious diseases, the inflammatory character of the endarteritic process as described by Klotz, could in many instances be determined.

CONCLUSIONS. The intima, although a non-vascular structure, is capable of suffering an acute inflammatory reaction.

This inflammatory infiltration occurs by the direct migration of the wandering cells from the lumen of the vessel.

An inflammatory reaction in the intima is not always accompanied by the presence of inflammatory cells in the remaining coats.

Furthermore, a simultaneous infiltration of the intima and adventitia by inflammatory cells may occur without any involvement of the media.

Accompanying the inflammatory reaction in the intima there are alterations in the elastica interna similar to those described in a previous paper.

Although we have had only the opportunity of observing early proliferative changes in the lesions studied, we, nevertheless, are of the opinion that ultimate repair is brought about by the continued proliferation of the fixed cells of the intima.

I am indebted to Dr. S. R. Haythorn for the specimens of nodular syphilitic meningitis.

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## THE ROENTGEN EXPERT WITNESS.

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COURTS of law depend upon facts. The legal value of medical testimony usually depends upon the introduction of a physician's expert opinion of an actual or a hypothetical case. There are rarely any tangible facts such as the exhibition of signed papers, defective machinery, etc. We may say that, generally speaking, expert medical testimony is inferential and based upon a physician's interpretation of actual or hypothetical symptoms, both objective and subjective. His opinion may be influenced, though not dishonestly, by this point of view or his medical training, experience and environment. The greater portion of the law with which the physician comes in contact is based upon personal damage suits. The extent of the injury to the plaintiff and its influence upon his health during the balance of his life, or for a lesser period, is the question which the physician is called upon to answer. The presence of actual damage to the permanent bony framework of the human body is of pertinent importance. This importance may be argued, but it is needless to argue that testimony which assures the judge and jury of actual bony damage or anatomical normality is of inestimable value.

Heretofore it has been possible to array upon both sides of a case medical talent capable of affirming or denying the actuality of a bony defect where the fracture was not compounded. Either diabolically or innocently, testimony adaptable to the lawyer's conception of his client's position could be secured.

Difference of opinion is not so much a matter of honesty or dishonesty as of temperament, environment, original concept, inheritance, public opinion and possibly least, knowledge of the subject. Therefore any medical testimony which presents tangible facts, either negative or positive, to a legal hypothesis is a valuable advance.

The apparent farcical yet perfectly legitimate inconsistency of the usual medical testimony is rarely apparent in Roentgen evidence.

The Roentgen-ray enters the medicolegal field with brilliant tangible evidence impossible of refutation if properly interpreted and adequately identified. No longer is it necessary to depend upon the mental conception of the surgeon who has merely inspected a patient's extremity when the actual shadows of the bony parts can be exhibited in court. While there remains the arguable question as to the importance or the influence or result of a fracture in a bone, there is no longer the necessity of medical conjecture as to its presence or absence.

The apparent forcefulness of Roentgen negatives does not necessarily imply their unconditional admission in courts of law. There is such latitude in the interpretation of even bony shadows as to seriously interfere with the unlimited bantering of such delicate scientific exhibits before a judge and jury of average citizens.

Let us consider a parallel in scientific evidence. For instance, a tract of land with a disputed boundary line its before the court. At the suggestion of the defendant the court appoints a disinterested surveyor to measure and plat the disputed land. The surveyor proceeds and then presents his testimony in court based upon the measurements made with surveying instruments. These instruments are necessary for the surveyor to come to exact conclusions as to the lay of the land and its dimensions, but he does not show his instruments to the jury. Another instance, a pathologist is asked to examine a tissue, let us say, the discharge of a supposedly pregnant woman. He proceeds to section the tissue, stain and examine it with the microscope. His opinion is the result of the use of these several instruments. Does he actually exhibit the microscopical slides to the judge and jury? No. Yet we constantly notice the actual exhibition of Roentgen negatives to the jury and permit the handling of these scientific instruments by jurymen who are wholly incapable to the least conception of shadow values.

The interpretation of Roentgen shadows is a matter of experience and a knowledge of anatomy and tissue density. The widely disseminated knowledge of photographic reproductions as to sharpness and accuracy of focus is not paralleled by contemporary Roentgen knowledge.

It is not best at present to assume any arbitrary position as to the admission of Roentgen testimony without the actual roentgenograms. There is little doubt but that the use of the actual Roentgen plates as a basis for Roentgen testimony does fortify the roentgenologist's evidence.

THE CONDUCT OF THE ROENTGEN EXPERT IN COURT. The Roentgen expert should limit his testimony to the facts which he believes his Roentgen evidence tends to prove. He should not

consider that his qualifications as a Roentgen expert permits him to exercise opinions which are distinctly matters of surgical judgment.

The Roentgen expert should qualify himself by submitting his experience of a number of years of actual Roentgen practice, based upon previous training under recognized authorities, he may recite his scholastic training in medicine and his affiliations with the usual medical societies, especially noting the organizations within his own specialty; his hospital appointments attest recognition of his standing within his own community. His literary pursuits may be meritorious but are more a valuation of his industrious proclivities rather than of his professional or expert ability.

It is well understood as a legal proposition that the credibility of Roentgen evidence depends upon the science, skill, experience and intelligence of the party taking the roentgenograms and testifying thereto.

The prejudice of trial attorneys toward clients frequently leads them to promote exaggerations in testimony. They may also plan to go beyond the facts of Roentgen evidence to establish extraordinary claims of disability. The Roentgen expert must be wary when the questioning is not sharply confined to the facts as he understands them from his Roentgen examination alone. Otherwise he may tend to subtract from the value of his Roentgen evidence by the undue comprehensiveness of his knowledge.

The Roentgen expert must maintain a neutral attitude and should not permit any prejudice or sympathy to influence his opinion. He must not consider his work infallible and the distortions and artifice which may appear in his exhibits must not be reflected in his testimony.

Roentgen evidence, properly interpreted and carefully presented to the court and jury, can wield such an incontrovertible influence that the roentgenologist must need maintain a calm, dignified, ethical attitude and appearance.

## A CLINICAL STUDY OF CHRONIC DIARRHEA.<sup>1</sup>

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THE relative frequency of various causes of diarrhea depends in large part upon the place in which cases are studied. Chronic

<sup>1</sup> Read at the Annual Meeting of the American Gastro-enterological Association, Baltimore, Md., May 10, 1915.

bacillary and amebic dysentery are relatively rare in New York and its environs, and chronic diarrhea is therefore a far more infrequent complaint than it is in some regions. We must also recognize that etiological statistics will vary with the observer on account of personal bias, and will depend upon the particular therapeutic field that he has cultivated which determines in part the type of case he sees. This series of 74 cases of chronic diarrhea which we have had the opportunity to study thoroughly in the office and laboratory is made up entirely of selected ambulant cases, selected in the sense that the condition of the patient justified thorough and repeated examination, and also because cancerous and luetic ulceration of the colon has been excluded from the series, as they rarely give rise to true diarrhea, but merely a discharge of blood and pus.

We are including under the term chronic diarrhea a constant or almost constant looseness of the bowels, a troublesome increase in the number of daily evacuations. In the accompanying table I have arranged what now seems to me the most satisfactory classification of the abnormal conditions that occasion chronic diarrhea. We must admit, however, that with improvements in our methods of study it may become necessary to recognize the importance of other conditions which are not included in this list. In this particular series some of the more unusual conditions did not occur.

TABLE I. ETIOLOGY OF CHRONIC DIARRHEA.

1. Achylia gastrica.
  2. Colitis.
    - (a) Catarrhal.
    - (b) Ulcerative.
      - Simple bacillary.
      - Amebic.
      - Luetic.
      - Cancerous.
      - Tubercular.
  3. Colonic stasis.
  4. Emotional excitability.
  5. Glandular disease.
    - Pancreas.
    - Thyroid.
    - Adrenal.
- The achylia group.

We shall confine the term achylia gastrica to those cases in which the test meal shows no free acid and the total acidity is twenty or under. The test meal is small in amount and shows little

TABLE II.

Number.	Age.	Sex.	Duration of symptoms	Gastric analysis.		Colitis.	Colonic stasis.	Other data.
				Free acid.	Total acidity.			
1	27	F.	3 years	60	80	.....	Marked	Neurotic.
2	65	M.	16 years	0	12	Atrophic	.....	Chronic nephritis.
3	40	M.	5 years	50	74	Ulcerative	.....	Non-amebic; hemorrhagic.
4	33	F.	3 years	0	20	.....	.....	Pulmonary tuberculosis.
5	47	F.	4 years	0	16	.....	.....	Goitre; acute thyrotoxicosis.
6	76	M.	6 years	0	10	Atrophic	.....	.....
7	42	M.	6 mos.	25	40	.....	.....	Graves' disease.
8	46	F.	1 year	20	35	Catarrhal	Marked	Neurotic.
9	38	M.	5 years	55	80	Catarrhal	Marked	.....
10	16	F.	1 year	..	..	.....	Marked	Rectum filled; spastic.
11	42	F.	2 years	0	12	Acute	No	Acute colitis in attacks.
12	43	F.	2 years	0	10	Catarrhal	No	.....
13	32	F.	3 years	0	15	Catarrhal	No	No relief from appendectomy.
14	39	F.	2 years	60	85	Catarrhal	No	Neurotic.
15	36	F.	1 year	0	15	.....	Marked	.....
16	38	F.	3 years	0	11	.....	.....	Tubercular enteritis.
17	35	F.	16 years	30	55	Ulcerative	.....	Amebic dysentery.
18	48	F.	6 mos.	35	70	.....	.....	Addison's (incipient).
19	49	M.	3 mos.	0	12	Catarrhal	.....	.....
20	68	F.	3 years	..	..	Ulcerative	.....	Non-amebic; hemorrhagic.
21	28	F.	5 years	..	..	.....	Marked	Spastic balls in rectum.
22	46	F.	10 years	65	80	.....	Marked	.....
23	45	F.	8 years	20	36	Catarrhal	.....	Chronic pancreatitis; stones.
24	33	F.	4 years	25	40	.....	.....	Emotional; diarrhea.
25	51	M.	1 year	35	65	.....	.....	Addison's (incipient).
26	30	M.	2 years	30	45	.....	Marked	.....
27	33	F.	6 years	0	15	.....	.....	Neurotic.
28	36	F.	8 years	40	60	.....	.....	Addison's (incipient).
29	29	M.	3 years	35	55	Ulcerative	.....	Non-amebic hemorrhagic.
30	35	F.	4 years	40	60	Catarrhal	Marked	Neurotic.
31	35	M.	6 years	32	45	Catarrhal	.....	Severe proctosigmoiditis.
32	29	F.	1 year	20	35	Catarrhal	Marked	.....
33	48	F.	2 years	34	50	Catarrhal	.....	.....
34	28	F.	10 years	0	12	.....	.....	Neurotic.
35	30	F.	3 mos.	20	52	Catarrhal	Marked	Spastic feces in colon.
36	42	F.	6 years	0	12	.....	.....	Neurotic.
37	64	M.	10 years	0	15	Ulcerative	.....	Cured by ipecac in five days.
38	47	M.	2 years	30	65	Catarrhal	.....	Severe proctosigmoiditis.
39	68	F.	1 year	..	..	Catarrhal	.....	Severe proctosigmoiditis.
40	62	M.	4 years	0	12	.....	Marked	.....
41	37	F.	5 years	30	47	Catarrhal	Marked	Severely toxic.
42	55	F.	5 years	..	..	Catarrhal	Marked	.....
43	30	M.	16 years	20	40	Ulcerative	.....	.....
44	38	F.	12 years	0	16	.....	.....	Graves' disease.
45	28	M.	6 mos.	..	..	Ulcerative	.....	Non-amebic; hemorrhagic.
46	44	M.	1 year	0	14	Catarrhal	.....	.....
47	34	M.	6 mos.	40	60	Catarrhal	.....	.....
48	31	M.	1 year	0	18	Catarrhal	.....	.....
49	29	F.	4 years	20	41	.....	Marked	Neurotic.
50	37	M.	3 years	29	55	Catarrhal	Marked	.....
51	38	M.	6 mos.	0	12	.....	.....	.....
52	53	M.	5 years	0	10	Catarrhal	.....	Pulmonary tuberculosis
53	55	M.	10 years	0	12	Catarrhal	.....	.....
54	33	M.	12 years	0	13	Catarrhal	.....	.....
55	35	F.	2 years	20	40	.....	.....	Pulmonary tuberculosis
56	35	M.	12 years	..	..	Ulcerative	.....	Amebic.
57	62	M.	6 years	0	20	Atrophic	.....	Cholelithiasis.
58	29	F.	1 year	30	50	.....	No	Hyperthyroidism.
59	32	F.	2 years	15	30	Catarrhal	Moderate	.....
60	34	F.	6 mos.	20	35	Catarrhal	.....	Graves' disease.
61	52	M.	1 year	20	35	Ulcerative	.....	Hemorrhagic; non-amebic.
62	37	M.	1 year	40	60	Catarrhal	Marked	.....
63	55	F.	7 years	15	25	.....	.....	Hyperthyroidism.
64	62	M.	3 years	0	15	.....	.....	.....
65	37	F.	6 years	25	40	.....	.....	Graves' disease.
66	61	M.	18 mos.	15	27	.....	.....	Addison's disease.
67	..	M.	3 years	0	20	Ulcerative	.....	Amebic.
68	35	F.	6 mos.	15	35	.....	.....	Addison's disease.
69	21	F.	5 years	30	50	Catarrhal	Marked	Spastic type.
70	17	F.	2 years	25	40	.....	Marked	.....
71	39	M.	2 years	35	55	Ulcerative	.....	Non-amebic; hemorrhagic
72	56	M.	8 years	0	9	Catarrhal	.....	.....
73	47	F.	1 year	30	55	.....	.....	Hyperthyroidism.
74	52	M.	3 years	15	45	Catarrhal	Intermittent	.....

chymification. Only on two occasions have I seen achylia disappear and free acid appear at a later period.

Of the 74 cases of chronic diarrhea in this series, 22 (or 34 per cent.) showed achylia gastrica. Diarrhea is not necessarily an accompaniment of failure of gastric digestion, as is shown by the fact that it is rarely seen in malignant disease of the stomach or after gastro-enterostomy for pyloric stenosis: and out of a total of 79 cases of achylia seen in my office, only these 22 had loose bowels. These statistics correspond closely with those published by Stockton<sup>2</sup> in a series of 132 cases of achylia. I have never seen a chronic diarrhea which I believed was explained by hyperchlorhydria. In those with diarrhea we might suppose there was a failure of pancreatic digestion, but this is contrary to our observation. The opinion that the diarrhea is of nervous origin is entirely untenable in a majority of cases. It is possible that in the constipation attending hyperacidity and the diarrhea of achylia we have some fundamental but as yet undiscovered fact of physiology, but at the present time we are, I think, forced to the conclusion that achylia is rather a predisposing cause of diarrhea, and that there is usually a direct exciting cause.

In studying these 22 cases I have been impressed with the number of times that concomitant conditions could be held accountable for the looseness of the bowels. In 8 cases examination disclosed a definite catarrhal colitis, and excellent results were secured solely by the treatment of the colitis. In 2 cases examination disclosed an amebic ulcerative dysentery, and the diarrhea was cured by ipecac therapy. In 3 cases there was colitis, and many organisms of the flagellate group were found in the fresh dejecta and gastric contents. Local treatment of the stomach and colon by irrigation resulted in temporary cessation of the diarrhea and the temporary disappearance of the flagellates, but no permanent relief. In 2 cases we have seen achylia gastrica in elderly men with atrophic colitis. In 4 cases there were periodic outbreaks of acute serous colitis characterized by the passage of enormous quantities of practically odorless fluid rich in serum albumin. In 2 cases there was a definite pulmonary tuberculosis and a considerable suspicion, although not entirely proved, of tuberculous enteritis. From these observations I am led to the opinion that achylia renders the individual more liable to chemical, mechanical, and microbial injury, which gives rise either to irritation of the colon with undue stimulation of peristalsis or to acute attacks of inflammation or to chronic changes in the mucosa.

My experience with the treatment of diarrhea associated with achylia has led me to view with considerable question some of the accepted ideas on the subject. So far as diet is concerned, I think

<sup>2</sup> AMER. JOUR. MED. SCI., 1909, cxxxviii, 157.

that ordinarily it has less affect than we have been led to believe. Foods which are ordinarily laxative, such as fruits and fats, may occasion or continue the bowel looseness more than in the normal individual. But, on the other hand, some patients do fully as well and many better on a diet in which there is an abundance of indigestible residue. The limitation of proteid food because gastric digestion is lacking gives no satisfactory clinical results. In the small group of cases where there are frequent outbreaks of acute colitis it is sometimes necessary to persist in a bland diet such as would be used in any subacute gastro-enteritis. Hydrochloric acid therapy has never proved of much temporary or any permanent value, although I have tried it repeatedly in different doses. I have never seen any good results with any form of enzyme therapy. Astringent medications have in the main given only temporary relief.

In a few instances I have seen remarkable results with massive doses of tannigen, 5 grains every hour day and night, for several days. These have all been in cases of profuse, watery diarrhea of long standing in which all other measures have failed. The more satisfactory results have been secured by the treatment of the colitis in those cases where it has been demonstrated.

**COLITIS GROUP.** In addition to the 8 cases of catarrhal colitis and 2 cases of amebic dysentery in achylia subjects the series showed 16 cases of chronic catarrhal colitis, 6 cases of non-amebic ulcerative colitis, and 5 cases of amebic ulcerative dysentery. The appearance of macroscopic mucus is not in itself sufficient evidence of a catarrhal condition. Mucus is essentially a protective substance, and is secreted when the mucosa is irritated. It seems to me the diagnosis rests on the history of repeated acute attacks of colitis, the presence of persistent tenderness over the course of the colon, the persistent admixture of mucus with or without pus and blood cells in soft feces, and the appearance of the mucosa of the rectum and sigmoid colon.

The diagnosis of amebic ulcerative colitis is best made by examination of scrapings made directly from the ulcerated areas with a dull curet. (In private and hospital practice I have repeatedly seen this demonstrated in cases of amebic dysentery when the report of the stools has been negative). Ulcerative non-amebic dysentery is comparatively rare in New York, according to my experience. Study of these cases has failed in every instance to demonstrate organisms of the dysentery group, although H. Strauss, of Berlin, in a recent article, reports positive agglutination findings with various bacilli of the typhoid dysentery group.

My experience with the treatment of the cases in which chronic colitis of various kinds has been demonstrated has been highly satisfactory. In the catarrhal cases I rely on a massive dose of bismuth subcarbonate, 3 ounces once a week, and daily rectal

injections of 8 to 16 ounces of a 10 per cent. solution of gelatin given at a temperature of 116° to 125° F. A diet rich in cellulose or the hemicellulose, agar-agar, is a most important means of preventing a recurrence of the catarrhal conditions. These cases have all done well with few exceptions in spite of gastric conditions. In the past six months I have seen two remarkable successes in intractable bloody dysentery of a severe form by the use of a preparation of the phenol group which the maker calls "trimethyl-methoxyphenol." It is said to be twenty times more bactericidal than carbolic acid, and its use in doses of 40 minims daily gives no evidence of toxicity, as it is not absorbed from the intestinal tract in the smallest amount. A rapid and permanent cure of these ulcerative dysenteries has been brought about by administration of this product by mouth and the addition of this preparation to gelatin injections. In my three previous cases of severe chronic bacillary dysentery the ultimate results were bad.

**EMOTIONAL DIARRHEA GROUP.** Neurotic conditions, as an explanation for chronic diarrhea are highly unsatisfactory, and only twice in this series have we been satisfied with this explanation. It is true that in many instances the patient is of a nervous temperament or has an irritable nervous system, and in one way or another this may increase the tendency to diarrhea. On the whole, however, such a diagnosis we would regard as exceedingly untrustworthy unless every other cause could be excluded and there was a most intimate association between exaggerated emotional states and abnormal peristaltic activity of the colon.

**STASIS GROUP.** A definite group or groups of cases complaining of diarrhea may with modern methods of diagnosis, especially the Roentgen-rays and sigmoidoscope, be found to have an underlying colonic stasis. Clinically, it has seemed to me we have three fairly well-marked varieties of this condition. This has been the sole condition found in 8 cases, and in all the diarrhea has been cured by treatment of the underlying constipation.

The first is a group of patients, usually young women, complaining of diarrhea, although the stools on examination are found to consist of small balls, apparently spastic feces. Examination of the sigmoid, in spite of several previous movements during the morning, shows a considerable filling with well-formed feces in the form of these tiny balls. Apparently we have to deal with a spastic irritability of the lower colon and a failure to empty the bowel completely at one time. Some of these cases are attended with an abnormal tightness of the sphincter muscle, with or without irritable fissures or hemorrhoids. On one occasion a single polyp was found high in the rectum, the removal of which resulted in the cessation of this rectal irritability.

The second group of cases may properly be designated fecal impaction, and fluoroscopic or roentgenographic examination shows



a dilated colon with a passage through a portion of the impacted area. This type of stasis constipation has been seen three times in this series, always in patients well along in years and of rather corpulent habit.

The third group is one which we have begun to recognize since using the Roentgen-rays as a routine in the study of these cases. There is stasis in a dilated cecum, usually prolapsed over the brim of the pelvis, which retains its contents an abnormal time—fermentative processes may be set up which give rise to intermittent or persistent diarrhea. It seems quite probable that this is one of the causes of the condition described by Schmidt and Strassburger as *Gärungsdyspepsia* and *Gärungcatarrh*. It is possible that diarrheas which have been said to depend on chronic appendix conditions are in reality brought about by conditions other than the inflamed appendix in the right iliac fossa. Diarrhea associated with chronic appendicitis is decidedly rare, and in those cases which have come under my observation it has persisted in spite of appendectomy, but has been relieved by the treatment of the coincidentally inflamed mucosa of the colon.

**THYROID GROUP.** In 9 cases there was ample evidence of hyperthyroidism, 4 showing definite exophthalmic goitre. As a rule, these patients do not seek relief for the intestinal disturbance but consult a heart specialist or neurologist. From my study of these cases I am convinced that we have to deal simply with hyperperistalsis, without failure of gastric or intestinal digestion, without colitis, without stasis. Every chronic diarrhea in a neurotic subject should be under suspicion of having its origin in a disturbance of thyroid function, and careful search should be made for the characteristic signs associated with hyperfunction of the gland.

**PANCREATIC GROUP.** Chronic pancreatitis and cancer of the pancreas with or without obstruction of the common bile duct are usually attended with large, soft, fatty stools, but by no means with diarrhea. In only one case in this series was chronic change in the pancreas demonstrated, and in this instance the condition was extremely severe, attended with glycosuria, with a high grade of intestinal putrefaction and colitis. I doubt that failure of pancreatic digestion is ever an adequate explanation of persistent diarrhea.

**ADRENAL GROUP.** Five cases in this series have seemed to me to represent an incipient form of Addison's disease, characterized by marked secondary anemia, with high lymphocyte count, disproportionate loss of flesh and strength, low blood-pressure, and a slight general bronzing of the skin without definite changes in the mucous membranes. In all of these cases it was possible to exclude thyroid disease, colonic stasis, failure of gastric digestion, and colitis. In 3 of these cases excellent results were secured by the use, over a long period, of nucleoproteid of the adrenal made by

Dr. S. P. Beebe, of Cornell University. Other adrenal preparations failed to have any effect on the diarrhea.<sup>3</sup> We have tried out this preparation in diarrheas apparently due to other conditions without success. Adams in his analysis of 97 cases of Addison's disease found that 31 showed definite improvement with a preparation of the adrenal gland given by mouth, while 16 were permanently relieved. We are, of course, dealing with an indefinite and complex group of cases, and the mere fact that these patients have survived for some years may throw some doubt on the suggestion of their having had disease of the adrenal gland. It is possible that we had to deal with a disturbance of adrenal function without actual destruction of the gland. The fact remains, however, that this preparation of the gland substance was specific in these 3 cases, while in general it has no constipating tendency.

SUMMARY. 1. Chronic diarrhea is a relatively infrequent affection. It may complicate any morbid condition, but in the study of this series of cases the attempt has been made to determine the factors responsible for the disturbance of bowel function.

2. Achylia gastrica occurs in about one-third of all cases, but is to be regarded as a predisposing cause of irritation and inflammation of the colon. The most satisfactory results in diarrhea associated with achylia were obtained by the treatment of colonic stasis by diet and the colitis by appropriate measures.

3. Colitis is not necessarily accompanied by chronic diarrhea, but particularly in the nervous seems to give rise to irritability of the colon, which causes frequent evacuations.

4. Colonic stasis may give rise to chronic diarrhea, and dietetic measures which increase peristaltic activity quiet the apparently already overstimulated bowels. Stasis is probably an important predisposing factor in colitis, for the permanent relief of the colitis depends largely on overcoming stasis.

5. Emotional excitability may at times be a factor in causing diarrhea, but nervous states are rarely to be regarded as the sole cause of chronic looseness of the bowels.

6. Hyperthyroidism frequently gives rise to a chronic diarrhea of moderate severity. It differs in this particular from the severe diarrhea, attended with emaciation and prostration, which accompanies destruction of the adrenal gland. It seems quite probable that the latter condition is more common than has been recognized, and is not entirely dependent on the destruction of the gland substance.

7. Success in the treatment of chronic diarrhea is peculiarly dependent upon the exhaustive study of the case by all diagnostic resources, particularly as a combination of factors is not infrequently responsible for the normal activity of the bowel.

# THE METABOLISM IN A CASE OF MYASTHENIA GRAVIS, WITH CONSIDERATIONS ON THE ADMINISTRATION OF CALCIUM AND OF GLANDULAR PREPARATIONS.

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AND

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A NUMBER of clinical and pathological observations in cases of myasthenia gravis have caused various authors to assign a prominent pathogenetic role in this disease to one or another of the organs of internal secretion as well as to the liver.

Oppenheim was the first to report a lesion of the *thymus* in this disease. In another case, Weigert found a lymphosarcoma of the thymus, associated with cellular infiltrations in the muscles, which he ascribed to metastases from the thymus tumor. A number of other cases have been reported in which some abnormality of the thymus was found at autopsy. Mandlebaum and Celler<sup>2</sup> have reported such a case, and in their excellent review of the subject are inclined to consider neoplasms of thymus origin as a possible pathogenetic factor in a certain proportion of the cases. A number of therapeutic suggestions have been based upon this association. Schuhmacher<sup>3</sup> claimed to have secured marked improvement after thymectomy in a case of Basedow's with myasthenic symptoms.

The association of myasthenia with *Basedow's* is not an uncommon one. Stern<sup>4</sup> in a recent article has cited a number of cases showing it. In his own case, tetanoid contractions of the fingers and pigmentation and bronzing of the skin were later associated with these conditions. He proposes to treat the disease by complete thymectomy and unilateral thyroidectomy.

Chvostek<sup>5</sup> ascribes importance to disturbances of the *parathyroids*. He attributes myasthenia to hyperfunction or dysfunction in contrast to the hypofunction of this gland, which he assumes to be the cause of tetany. The changes in the thymus so frequently found in myasthenia, he believes are of no pathogenetic

<sup>1</sup> Work done under tenure of the Theodor Escherich Fellowship in Pathology.  
<sup>2</sup> Jour. Exp. Med., 1908, x, 308.

<sup>3</sup> Mitt. a. d. Grenzgeb. d. Med. u. Chir., vol. xxv.

<sup>4</sup> Neurol. Centralbl., 1914, p. 409.

<sup>5</sup> Wien. klin. Wchnschr., 1908, xxi, 37; Lubarsch and Ostertag's Allg. Pathol. u. pathol. Anat. d. Mens. u. Tiere, 1908.

importance. The weight of experimental evidence is against his theory.<sup>6</sup>

We have referred to the finding of bronzing and pigmentation of the skin in myasthenia by others. This was present in our case as well. It is well known that in dogs muscular weakness and increased skin pigmentation follow adrenal extirpation and that the pigmentation can be made to disappear by infusions of epinephrin. Therefore, an etiological connection between an *adrenal* lesion and the myasthenic symptom-complex must be considered possible. The high blood-pressure in our case might also be taken as further evidence of this connection were it not that the experimental facts in regard to the connection between disturbances of blood-pressure and adrenal lesions are contradictory.

The urine in our patient showed signs of a nephritis, the quantity and specific gravity were approximately normal, and the nitrogen excretion was sufficient. We are inclined to believe that the kidney lesion was comparatively unimportant and not in itself sufficient to explain the high blood-pressure.

At the time our investigations were made, previous publications on the subject led us to expect distinct variations from the normal in the metabolism of our patient. Spriggs<sup>7</sup> had found the creatinin excretion decidedly below normal in his patient. Pemberton<sup>8</sup> was able to corroborate this in one case, in which he found also a marked loss of calcium with a normal nitrogen balance. Diller and Rosenbloom<sup>9</sup> have quite recently published a case in which they got the same results for calcium and creatinin, accompanied, however, by a negative nitrogen balance. Kaufmann<sup>10</sup> in his patient investigated principally the nitrogen metabolism and the ammonia excretion. He found that exercise caused a decrease in the retention of nitrogen, and if continued, a loss together with increased excretion of ammonia. In his case there was, however, disease of the liver.

In our case the metabolism of nitrogen, phosphorus, sulphur, calcium and magnesium, and the ammonia and creatinin excretion were studied while at rest, with exercise to the point of exhaustion, during the administration of epinephrin (Parke, Davis & Co.), and of thymus<sup>11</sup> gland, followed immediately by a control period and also with prolonged administration of calcium. The calcium was given with the intention of studying its effect on the symptoms and on the loss of calcium we anticipated in the earlier periods. We wished to observe the effect of epinephrin and of thymus on the clinical symptoms and on the metabolism.

<sup>6</sup> Biedl, A., *Intere Sekretion*, 24 ed., 1913, i, 108.

<sup>7</sup> *Quart. Jour. Med.*, 1907, i, 68.

<sup>8</sup> *AMER. JOUR. MED. SCI.*, 1910, cxxxix, 816. In Pemberton's work the composition of the food was obtained by computation, not by analysis.

<sup>9</sup> *AMER. JOUR. MED. SCI.*, 1914, cxlviii, 65.

<sup>10</sup> *Monatsch. f. Psych. u. Neur.*, 1906, xx, 209.

<sup>11</sup> This and the other glandular substances given were Armour & Co.'s preparation.

A study of the tables shows that in our case, except for the creatinin, there was no striking variation from the normal in any of the constituents studied during any of the experiments. There was throughout a retention of calcium, of magnesium, and of sulphur, and except for a very slight loss in the last period, a substantial retention of nitrogen and phosphorus. There was no disturbance of the ammonia excretion even during the exercise period (Period II), although at this time there was less retention of nitrogen. There is, therefore, contrary to the opinion held by Kaufmann, no evidence of an acidosis in our case. Period IV shows a slight increase in the retention of all the constituents. This was probably due in part to poor marking off of the stool, as the daily weight of the dried feces was less than in the other periods. During thymus feeding there was an increased retention of nitrogen and of phosphorus. Three days before the beginning of the period of calcium administration (Period X) the patient had a slight intestinal disturbance for two days, accompanied by abdominal cramps and diarrhea. It is probable that the slight loss of nitrogen and phosphorus is connected with this. During this period almost all of the additional calcium fed to the patient was excreted.

In common with previous observers we found a low creatinin excretion. This shows best in the creatinin coefficient, which averages 4.8 mgs. creatinin-nitrogen per kilo (normal 7-11 mgs.), while the ratio excreted to the total nitrogen averages 3.6 per cent., (normal 3.9 per cent.). During the thymus period and the calcium period creatin was excreted in noticeable amounts.

The work of Halpern has been made available to us very recently by a translation which we owe to the kindness of Dr. Lowenthal. In two cases of myasthenia, Halpern found marked retention of nitrogen, phosphorus, and lime, with a normal ammonia excretion. In his last published case,<sup>12</sup> during a five-day experiment, the daily intake (the composition of the diet appears to have been computed) and balance were as follows:

	Intake.	Retention.
Nitrogen . . . . .	17.30 gms.	3.00 gms.
Phosphorus . . . . .	2.40 gms.	0.13 gm.
Calcium oxide . . . . .	3.65 gms.	1.69 gms.

The retention, it will be seen, closely resembles our results, except that the calcium retained by his patient is very much greater than in our case. The weight of the woman on whom the experiment was made is not mentioned, nor are any other clinical data given in his paper. In the absence of these it would be idle to attempt to explain the quantitative differences between his results and our own.

Prolonged administration of calcium, of ovarian substance, of

<sup>12</sup> Halpern, *Miecz. Medycyna*, 1912, xlvii, 914.

testicular substance and of thymus had no apparent effect on the clinical course in our case. While the patient was receiving epinephrin she developed cardiac palpitation and tachycardia after each administration, together with flushes and a feeling of weakness. It is clear that the result of our work offers no support for the administration of calcium in the treatment of this disease, as suggested by Pemberton. In the absence of clinical improvement from the administration of thymus gland, the increase in the retention of nitrogen and phosphorus do not constitute an argument for its use. Nor have we any evidence upon which to recommend the use of ovarian or testicular substance, while the use of epinephrin was clearly harmful in our patient.

**CLINICAL DATA.** S. S., aged forty-nine years; female. Admitted to the neurological service of the Mount Sinai Hospital, May 2, 1912.

Has one child alive and well. No other pregnancies. Last menstruation October, 1911. For the past two years troubled by epigastric oppression coming on a few minutes after eating and persisting for several hours, accompanied by eructations of gas. Has lost twenty-two pounds in last two months. About six weeks before admission she noticed drooping of right eyelid and inability to raise it at will, followed shortly after by the same manifestations in the left lid. At this time she once fell to the ground from weakness. About ten days before admission she noticed difficulty in swallowing, which became more and more marked toward the end of the meal. About three days later she noticed difficulty in speaking and feeling of heaviness and thickness in the tongue. The arms are gradually becoming weaker; the muscles of the neck have been weak since the onset of illness.

*Physical Signs.* Looks prostrated; sallow; skin negative.

July 5. *Eyes.* (Dr. Wolff). Incomplete ptosis of right eye; ocular motility in all directions restricted in varying degree, involving third, sixth, and fourth nerves of both sides. Lower branches of left facial nerve paretic. Fundi normal. Diagnosis: incomplete external ophthalmoplegia.

Very slight rigidity of neck. Teeth carious; pyorrhea alveolaris.

*Lungs.* Percussion note hyperresonant. Respiratory murmur distant and weak; expiration is low pitched and prolonged. Few moist rales at bases.

*Heart.* Rapid. First sound has lost most of its muscular quality. No enlargement.

*Liver and Spleen.* Negative.

*Abdomen.* Lower poles of both kidneys felt; otherwise negative.

*Extremities.* Inexhaustible clonus in right ankle. Deep reflexes generally exaggerated.

*Sensations.* Normal. Speech slow and difficult; enunciates poorly. Pronunciation of labials good, that of linguals somewhat impaired.

Swallowing difficult, no regurgitation through nose. Apparently some paresis of soft palate.

July 8. Less drooping of right eyelid. Voice stronger. Tongue can be fully protruded. Pulse of good quality and tension. The condition varies from day to day; at times voice becomes very weak and husky; eyelids droop and she says it is difficult to masticate because of weakness of lower jaw. No true fibrillation of tongue. Diagnosis at present between myasthenia gravis and organic bulbar-pontine lesion, with a probability of its being the former.

July 18. General condition improving; musculature becoming stronger. Speaks very much more clearly; can control eyelids with more power. Formerly when taking fluids by means of siphon tube, had to rest after an ounce or two. Now takes several ounces without resting. Pulse tension better. Her condition does not vary so much from day to day.

July 27. Electrical reaction. No reaction of degeneration. Muscles respond promptly to normal faradic current and rapid stimulation causes no fatigue. Patient thinks that power in hands is much improved after stimulation. On raising the arms at right angles, myasthenic reaction becomes very marked.

August 9. Myasthenic reaction in masseter, facial muscles, triceps, and pectoralis major marked.

August 27. Still partial ptosis of right eye, varying from day to day and at various times of same day. Feels much better. The exhaustion on voluntary movement no longer perceived. Voice less nasal. No dysphagia, no diplopia, etc. Since yesterday, slight exhaustion in supporting extended upper extremities.

September 13. Gradually improving. Ptosis and muscle exhaustion still occur at times. From this time until the patient left the hospital in January, 1913, there was no important change in her general condition. The myasthenic condition at times becomes more pronounced for a short period. In December bronzing of the skin was noted. This gradually increased and was most marked on the knees and elbows. There was no pigmentation of the mucous membranes. Several times during her stay in the hospital the bowels were loose for several days at a time. This condition yielded readily to treatment with opium and bismuth. Twice peculiar attacks were noted. These lasted fifteen to twenty minutes. She suddenly became very weak, dyspneic, broke into a cold sweat. The face and hands became cyanotic. The pulse was rapid, weak, and apparently low tension, but remained regular. Respiration was of the abdominal type, the chest being practically motionless.

*Urine:* Sp. gr., 1012 to 1026. Most of the examinations showed a faint trace of albumin, an occasional hyaline cast in the centrifuged specimen; no sugar. Daily quantity, 425 to 1100 c.c.

*Wassermann* and *von Pirquet* negative.

*Blood Count.* Leukocytes, 9000; small lymphocytes, 21 per cent.; large lymphocytes, 7 per cent.; eosinophils, 3 per cent.; polymuclears, 70 per cent.

*Blood-pressure* (summarized from several observations). Systolic, 190 to 215; diastolic, 140 to 170. Pulse pressure, 35 to 65.

The weight varied between 48.5 and 51 kilos.

The patient has been under observation since discharge from the hospital.

In March, 1913, diffuse pigmentation of buccal mucous membrane appeared. The strength of the muscles of the neck improved, but her condition otherwise remained unchanged. There was from time to time a transient improvement in her condition, so that she was able to walk about the room with assistance and at times alone.

Early in 1914 there was a period of marked improvement lasting six months continuously. Since September, 1914, at intervals of about a month, she became worse for a few days at a time. The muscles, especially of tongue, mouth, and eyelids, then became weaker; she felt generally weaker and had repeated flushes. During these periods she had a sensation of epigastric oppression, and the liver was tender and palpable. On several occasions there was nausea. Reflexes remained unchanged. The systolic blood-pressure was between 160 and 200. Thymus gland was given at home for two months immediately after the patient left the hospital. During the past two and a half years she received ovarian substance on and off for long periods, 5 grains being given three times daily. Dried-beef testicle was also given in the same dose for eight or nine months.

The patient died March 21, 1915, as the result of an acute bronchopneumonia. An autopsy could not be performed.

To sum up the clinical features, we have a characteristic case of myasthenia gravis presenting also an occasional transitory attack of marked dyspnea and tachycardia. Unusual symptoms are the extremely high blood-pressure and the increasing dermal pigmentation and pigmentation of the buccal mucous membrane.

**EXPERIMENTAL DATA.** The patient during each of the metabolism periods and for at least three days preceding was fed on the Folin<sup>13</sup> test diet. The amount taken was carefully measured and an equal amount preserved daily for analysis. This was shaken with about 1 per cent. of toluol, placed on ice, and a combined sample made up for analysis at the end of each period. Urine and feces were also analyzed for the whole period, except that nitrogen, ammonia, creatin, and creatinin estimations in the urine were made for each day separately. Feces were marked off by means of carmin. All analyses were made in duplicate, and



the figures given are averages from pairs of closely corresponding results. The analytical methods used have been given in detail by one of us in an earlier paper,<sup>14</sup> the only variation being that feces, food, and urine were all ashed in platinum as a preliminary to the McCrudden method. Except during Period II the patient was kept in bed.

Period I. Duration, six days—July 24 to 30.

Period II. Duration, six days—August 1 to 7. Walked several times a day until exhausted; aggregate about 500 meters daily.

Period IV. Duration four days—August 14 to 17. From August 11 to 17 inclusive, 10 minims of 1-1000 epinephrin were given hypodermically three times daily.

Period VI. Duration six days—September 1 to 7. Five grams of thymus gland were given thrice daily during this time.

Period VII. Duration, seven days—September 7 to 14. Thymus gland was given from September 14 to November 18 in the same dose as before. From November 15 to December 26, 6 gms. of calcium lactate were given daily in four doses.

Period X. Duration six days—December 18 to 22. On account of slight intestinal disturbance preceding it the food mixture was diluted with half its volume of water. The calcium lactate contained 0.7734 gms. CaO in the daily dose. The feeding mixture also contained more lime than before, so that the amount of this substance given was about double that during the other periods studied.

The results of the analyses follow and are averaged for each period in grams per diem:

TABLE I.

Period.		I	II	IV	VI	VII	X
Food	N	8.082	8.86	9.32	9.86	9.75 <sup>15</sup>	9.87
	S	0.791	0.876	0.938	0.952	1.048	1.238
	P	0.805	0.999	0.948	1.037	1.033	1.037
	CaO	1.084	1.137	1.145	1.181	1.112	2.207
	MgO	0.299	0.336	0.339	0.328	0.409	0.331
Feces	N	0.443	0.766	0.255	0.997	0.755	0.8
	S	0.042	0.067	0.038	0.098	0.072	0.105
	P	0.175	0.223	0.114	0.246	0.18	0.328
	CaO	0.511	0.939	0.371	0.767	0.62	1.548
	MgO	0.082	0.245	0.102	0.174	0.137	0.213
Urine	N	5.377	7.07	6.335	5.441	6.659	9.458
	S	0.616	0.495	0.569	0.518	0.605	0.765
	P	0.602	0.622	0.416	0.472	0.611	0.899
	CaO	0.128	0.136	0.112	0.192	0.192	0.34
	MgO	0.045	0.039	0.06	0.076	0.08	0.109
Balance	N	+2.262	+1.023	+2.73	+3.422	+2.336	-0.388
	S	+0.133	+0.314	+0.31	+0.336	+0.371	+0.368
	P	+0.028	+0.154	+0.386	+0.319	+0.242	-0.19
	CaO	+0.455	+0.062	+0.662	+0.221	+0.3	+0.319
	MgO	+0.172	+0.052	+0.176	+0.078	+0.192	+0.009

<sup>14</sup> Bookman, A., Amer. Jour. Dis. of Children, 1914, vii, 436.

<sup>15</sup> Computed.

TABLE II.

Period.	I	II	IV	VI	VII	X
Total nitrogen . . . . .	5.38	7.07	6.33	5.44	6.66	9.46
Ammonia nitrogen . . . . .	0.42	0.396		0.367	0.466	0.556
Creatin . . . . .	0.046	0.036		0.148		0.202
Total creatinin . . . . .	0.653	0.571	0.71	0.613	0.518	0.805
Total creatinin as nitrogen . . . . .	0.242	0.212	0.26	0.227	0.192	0.299
Percentage of total creatinin, nitrogen to total nitrogen . . . . .	4.5	3.0	4.1	4.2	2.8	3.2
Milligrams of creatinin nitro- gen per kilo body weight . . . . .	4.7	4.1	5.1	4.7	4.0	6.0

SUMMARY. This case of myasthenia gravis presented as unusual symptoms bronzing of the skin and pigmentation of the buccal mucous membrane and high blood-pressure.

The metabolism of calcium, magnesium, phosphorus, sulphur, and nitrogen and the ammonia excretion were studied, with the patient at rest, while taking exercise, during the administration of epinephrin, of thymus gland, and of calcium, and presented no abnormal features. The excretion of creatinin was below normal. There was at times a considerable excretion of creatin.

Ovarian and testicular substance were also administered. Neither the glandular preparations nor the calcium appeared to have any influence upon the clinical course.

## REVIEWS

PRINCIPLES OF HUMAN PHYSIOLOGY. By ERNEST H. STARLING, M.D. (Lond.), F.R.C.P., F.R.S., HON. M.D. (Breslau), HON. Sc.D. (Cambridge and Dublin). Second edition; pp. 1271; 566 illustrations, 10 in colors. Philadelphia and New York: Lea & Febiger, 1915.

PERHAPS none of the fundamental subjects in medicine has undergone more radical changes of late than has physiology. For this reason it is particularly gratifying to welcome a new and thoroughly revised edition of Starling's *Text-book of Physiology*, long regarded as one of the standard works on this subject.

In this new edition the author has wisely eliminated some of the less important subjects that appeared in the first edition, thereby reducing somewhat the size of the volume. At the same time, however, he has brought the subject matter thoroughly up-to-date by revising and even rewriting many of the sections and by introducing much new material. Among the chapters that have been decidedly improved by rewriting, are those on the circulation and those on the voluntary muscles. The additions embrace invariably live subjects that have proved to be of far-reaching importance and wide-spread interest. For example Starling discusses carefully such topics as vitamins, the human cardiogram, the various cardiac nodes, etc., and has added entire chapters dealing with the innervation of the bronchial musculature and the nutrition of the brain. To enumerate in detail all the additions and changes is out of the question. Suffice it to say that in this new edition, the author has set forth that which is best and most modern in physiological teaching.

Throughout the entire book one is impressed by the fact that Starling never fails to emphasize the fundamental relationship that exists between physiology and the clinical side of medicine. As a result of this attitude he has introduced into physiology a clinical interest that should prove helpful and stimulating to both student and practitioner.

G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics in the Jefferson Medical College, Philadelphia, and LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics in Jefferson Medical College, Philadelphia. Vol. III, September, 1915. Pp. 307; 26 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

IN *Progressive Medicine* for September, 1915, William Ewart has a most instructive article of nearly a hundred pages on the heart, lungs, and other intrathoracic viscera, including the thyroid. Ewart's medical contributions have distinct literary merit; like many of his countrymen he takes the trouble to write well, thereby setting an example that might to advantage be followed by a large number of present-day medical writers. Ewart in this contribution has not confined himself to purely clinical subjects, but has taken up at some length many important physiological and pathological problems. Dermatology and syphilis are discussed by William S. Gottheil. He lays particular stress upon the treatment of psoriasis, furunculosis, dermal tuberculosis, and favus and ringworm of the nails. The few pages he devotes to syphilis are almost wholly taken up by a discussion of the present status of syphilis therapy. As has always been the case heretofore, Edward P. Davis furnishes a most exhaustive review of obstetrics. In addition to discussing pregnancy, eclampsia, the placenta, labor, and the puerperium, he devotes considerable space to obstetric surgery and to diseases of the newborn. The article on diseases of the nervous system, which concludes the volume, is worthy of its eminent author, William G. Spiller. Without placing undue emphasis on any one subject, in the space of fifty-eight pages Spiller seems to have touched upon nearly every new and important subject in neurology.

G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics in Jefferson Medical College, Philadelphia, and LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. IV. December, 1915. Pp. 421; 79 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

VOLUME IV, the December number of *Progressive Medicine*, opens with a long article by Edward H. Goodman on diseases of the digestive tract and allied organs. At the outset he lays great

stress on oral sepsis and its relation to disease. Among the many other important subjects which he particularly emphasizes should be mentioned: studies on gastric function; gastric ulcer and carcinoma; achylia gastrica; syphilis of the stomach; duodenal ulcer; constipation; colitis polyposa; chronic appendicitis; functional tests for hepatic insufficiency; cholelithiasis; pancreatitis; and pancreatic functional tests. J. Harold Austin's contribution on diseases of the kidneys is an admirable critical review of the enormous amount of work that has recently been done on renal function. In addition, he describes various types of nephritis, uremia, renal tuberculosis, and hydronephrosis. The surgical aspect of renal diseases is dealt with by Charles W. Bonney, who also takes up diseases of the ureter, bladder, prostate, and genito-urinary diseases in general. Of the many noteworthy contributions that each year appear in *Progressive Medicine*, there are none more deserving of favorable comment than the careful, critical reviews furnished by Joseph C. Bloodgood. His present article, dealing as it does largely with the subjects of shock, anesthesia, wounds, infection, fractures, and dislocations, is particularly interesting, since it has given him an opportunity to describe first aid and military surgery, with special reference to the lessons learned in the present European conflict. The volume concludes with a practical therapeutic referendum by H. R. M. Landis, in which he discusses many therapeutic agents that are of particular interest at present, such as the various sera, benzol, corpus luteum extract, emetine, kaolin, liquid paraffin, pituitrin, and vaccines.

Without a doubt, each year the contributions to *Progressive Medicine* are more thoughtfully and carefully prepared; the result is that with every new volume this quarterly becomes more and more a necessity to the physician who strives to keep abreast of the times.

G. M. P.

NOTES ON DENTAL METALLURGY. By W. BRUCE HEPBURNE, L.D.L. (Glasgow), Lecturer on Dental Metallurgy and Visiting Dental Surgeon in the Glasgow Dental College and School; Member of the Dental Examining Board of the Royal Faculty of Physicians and Surgeons. Second edition. New York: William Wood & Company.

THE present revised edition of this book which the editor now presents is a valuable contribution to dental metallurgy, and was probably prompted by the manifest changes in the knowledge and views now held regarding amalgams and cements. The chapters devoted to these subjects and alloys clearly and ably express the most recent ideas. The field that obtains strictly to dental metallurgy is important but rather restricted. This small book has been most carefully written throughout, and can be recommended.

P. L. L.

THE HOUSE-FLY, *MUSCA DOMESTICA* LINN. ITS STRUCTURE, HABITS, DEVELOPMENT, RELATION TO DISEASE AND CONTROL. By C. GORDON HEWITT, Dominion Entomologist of Canada; formerly Lecturer in Economic Zoölogy in the University of Manchester. Pp. 382; 104 illustrations, partly in colors. Cambridge University Press, Zoölogical Series.

THIS work represents the development of a subject which was presented by the author in a series of papers during the years of 1907, 1908, 1909. It is not designed to be a popular treatise on the house-fly, but is intended to serve the more exacting needs of "entomologists, medical men, health officers, and others similarly engaged." Doubtless it will be very welcome to those whose business it is to fight the diseases propagated by our most common insect pest. The scope of the book is indicated by the titles of its six parts. They are: (1) structure and habits of the house-fly; (2) breeding habits, life history, and structure of the larva; (3) the natural enemies and parasites of the house-fly; (4) other species of flies frequenting houses; (5) the relation of house-flies to disease; (6) control measures. Nearly one-third of the book is devoted to a consideration of the last two topics. Experiments showing the nature of the dissemination of various disease-producing bacteria are described and illustrated. Practical means for reducing the numbers of flies are considered. There is an excellent bibliography, together with author and subject indexes. C. E. McC.

A TEXT-BOOK OF MEDICAL CHEMISTRY AND TOXICOLOGY. By JAMES W. HOLLAND, M.D., Emeritus Professor of Medical Chemistry and Toxicology, Jefferson Medical College, Philadelphia. Fourth edition; pp. 678; 116 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE problem confronting every author of a text-book is to keep its successive editions abreast of the times. Although but four years have passed since the third edition of Holland's *Medical Chemistry and Toxicology* appeared, still many new changes were necessitated in the revision of the present work.

The rapidity with which we are making progress in these fields is indicated by an increase of 147 pages over the previous volume. With the exception of the opening paragraphs, which have been omitted, the first 215 pages are practically unchanged; in fact, the same general plan of the previous edition has been continued in this fourth printing; one which seems most satisfactory. Extensions to the chapters on radium, thorium, uranium, and vanadium cover the field very well. The newer organic compounds of arsenic,

the constitution of the carbohydrates and glucosides, the synthetic local anesthetics allied to cocain, the protective enzymes, the hormones, and an entire new chapter on feces are all subjects of timely and valuable information to the reader. A number of new tests have been added, including those in connection with names of Seleivanoff, Wassermann, Vollhard, Harvey, Benedict, Folin, Hart, Russo, Tsuchiya, Fromer, Abderhalden, etc. Whether all of these tests should occupy a position in a standard text-book is of course open to debate. Some of them still operate on uncertain grounds. A more minute description of the details in their execution would, we believe, be of value to the student of medicine who goes to this book as a laboratory guide.

The work remains an excellent exposition of the subject. It covers the ground in a crisp manner and furnishes a foundation for those who choose to build upon it. The author is to be congratulated upon the revision.

T. G. S.

ROENTGEN RAYS: HOW TO PRODUCE AND INTERPRET THEM. By HAROLD MOWAT, M.D. (Edin.), Temporary Lieutenant R. A. M. C. At present Officer to Roentgen-ray Department, Meerut Indian General Hospital; Radiographer to Metropolitan Hospital and Royal Chest Hospital. Pp. 204; 106 illustrations. New York: Oxford University Press, 1915.

It is unfortunate that this book should have gone to press just at this time, when the author's military service has evidently been the cause of its completion in a very hurried manner. He states in the preface that the "book is written for those who have little or no knowledge of the subject of Roentgen rays." Unfortunate, again, since it is for this class of readers that the greatest accuracy is essential, and the book is certainly not free from inaccuracies, in addition to being very incomplete. We cannot conscientiously recommend it to this class of readers, to say the least. The criticism of a roentgenologist would begin at the title and continue to the end. The illustrations in connection with the thorax and digestive tract are exceedingly poor.

H. K. P.

HEADACHE. By DR. SIEGMUND AUERBACH, translated by ERNEST PLAYFAIR, M.B., M.R.C.P. Pp. 208. London-Oxford University Press.

THIS small volume is a splendid scientific discussion of the important symptom of headache in all its various phases and manifestations. It well merits a careful study.

H. J. M., JR.

HUMAN PHYSIOLOGY. By LUIGI LUCIANI, Director of the Physiological Institute of the Royal University of Rome. Translated by FRANCES A. WELBY. In five volumes. Vol. III. The Muscular and Nervous Systems. Edited by GORDON M. HOLMES. M.D. Pp. 558; 141 illustrations. New York: Macmillan Company, 1915.

THE third volume of the monumental work of Luciani excels the two volumes which have previously found their way into English on account of the fact that the translation is from the fourth Italian edition, which has appeared since the English translations of Volumes I and II. The subject matter is thus brought up to 1913.

The book embraces the following subjects: general physiology of muscle; mechanics of the locomotor apparatus; phonation and articulation; general and special physiology of the nervous system. At the end of each chapter is a short bibliography containing only most carefully selected references. References to recent English literature have also been introduced. The volume, therefore, on account of the thoroughness with which the subjects have been considered and the brief but valuable bibliography, serves as a most splendid reference book.

In this volume, perhaps more so than in any of those which have thus far appeared, one appreciates the wonderful mentality of its illustrious author. The logical sequence of the data presented, the conservatism of opinion upon mooted subjects, the philosophical attitude both broad and analytical, and the clearness of expression, all impress the reader with his greatness. The work for years to come will remain a much-used book of reference, will live as do the works of Müller and those works edited by Schäfer. The reader is seldom conscious of being in the hands of a translator; the style is clear and free.

E. L.

AN ESSAY ON HASHEESH, INCLUDING OBSERVATIONS AND EXPERIMENTS. By VICTOR ROBINS, Contributing Editor, *Medical Review of Reviews*; Pharmaceutical Chemist, Columbia University. Pp. 83. New York: Medical Review of Reviews.

THIS essay on hasheesh is made the cloak for an interesting bit of observation and experimentation. The historical, pharmaceutical, and therapeutic considerations of the drug are followed by an account of the results of its administration, in intoxicating dose, to a number of persons, including the author himself.

A. A. H.



# PROGRESS OF MEDICAL SCIENCE

## MEDICINE

UNDER THE CHARGE OF

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AND

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**The European Bed-bug as a Carrier of Disease.** — D. THOMSON (*Annals Trop. Med. and Parasitol.*, 1914, viii, 19) points out the advances made in the study of the transmission of such tropical diseases as malaria, yellow fever and filariasis. Similar work has, he says, been neglected in connection with diseases of the temperate climates. The present study deals with the European bed-bug. Thomson first studied 184 bugs as controls; the majority of them were adult bugs which had presumably fed upon human beings who may have been diseased, and were not, therefore, proper controls in the strict sense of the term; 107 of these were examined for acid-fast bacilli with the Ziehl-Neelsen stain, the remaining 77 being stained with Giemsa's stain. No acid-fast bacilli were found and no protozoa. In feeding the bugs on diseased individuals the following results were obtained: One hundred and five bugs fed on lepers and 35 caught on the mattresses of lepers were examined. In none were acid-fast organisms found. Five bed-bugs were fed on an advanced case of Hodgkins' disease. All developed within eight days a gravis, mouldy growth over the body and examination showed them to be infected with a mycelium and spores. However, 22 bugs fed on an early case of Hodgkins' disease showed no such condition, even thirteen days after feeding, though 65 per cent. of them showed "Chlamydozoön-like bodies." Thirty bugs fed on a patient with myeloid leukemia were studied, the examinations being made four to nineteen days later. All showed Charcot-Leyden crystals in intestines and feces. Fifty per cent. of these bugs also contained the "Chlamydozoön-like bodies." The latter were also found in 60 per cent. of the bugs which fed on a patient with lymphoid leukemia and in 43 per cent. of those allowed to feed on a

patient with sarcoma of the ileum. The results with a few bugs fed on a cancerous patient were entirely negative. While Thomson's results are largely negative, there is need for further study, he says.

**The Relation of Bile Pigments to Hemoglobin.**—J. O. W. BARRATT and W. YORKE (*Annals Trop. Med. and Parasitol.*, 1914, viii, 509) have made an experimental study on the rabbit of the relation of bile pigments to hemoglobin. Under ether anesthesia, a cannula was inserted into the gall-bladder; the common duct was ligatured. The bile was collected for a certain period of time and then homologous hemoglobin solutions were injected intravenously. The bile was again collected and its concentration was compared with that collected during the control period by means of a Zeiss comparison spectroscope. Barratt and Yorke summarize their findings as follows: Consequent upon intravenous injection of hemoglobin solution there is a distinct and immediate increase not only in the concentration of bile pigment but also in the amount of bile pigment excreted. During the three or four hours following the injection the amount of pigment excreted may increase from four to six times the amount found before the injection. Two hypotheses may be advanced to explain this increase, (1) that the hemoglobin injected is actually converted by the liver into bile pigment, or (2) that it merely stimulates the liver cells to increased production of bile pigment. Against the first hypothesis is the fact that the increase of pigment is not so great as might be anticipated from the relatively large quantity of hemoglobin introduced into the circulation and the consequent high degree of hemoglobinemia resulting (up to 20 per cent.). The amount of hemoglobin found in the plasma of normal rabbits is between 0.02 and 0.05 per cent. This fact seems to indicate that the degree of red-cell destruction normally occurring in the living animal is slight. Assuming that the pigment of normal bile is derived entirely from hemoglobin set free by the disintegration of erythrocytes normally occurring in the living animal, then it is rather surprising that when the degree of hemoglobinemia is increased four hundred times, the amount of bile pigment is augmented only sixfold at the most. Furthermore, as Yorke and Nauss have shown, the mere introduction of homologous hemoglobin solution into the veins of normal rabbits is not enough to produce jaundice. The hemoglobinemia gradually disappears, leaving the blood plasma clear and colorless without any trace of bile pigment. Barratt and Yorke attempt to apply their results to blackwater fever. Since from these experiments it appears that intravenous injection of hemoglobin results in an increased excretion of bile pigment it would seem that the icterus almost invariably observed in blackwater fever cannot be attributed solely to hemoglobinemia.

**An Improvement in the Phenolphthalin Test for Occult Blood in the Feces.**—I. BOAS (*Deutsch. med. Wchnschr.*, 1915, xli, 549) describes a modification of his recently proposed method of performing the phenolphthalin test for occult blood in the feces. The reagent is prepared as follows: 25 gm. of potassium hydrate are dissolved in 100 c.c. of distilled water; 1 gm. of phenolphthalin is added, and the mixture is taken vigorously. After solution is complete, powdered metallic

zinc is added, and the preparation is boiled in an Erlenmeyer flask until the fluid is completely decolorized. After cooling, distilled water is added to the original volume and the solution is filtered. The filtrate is water-clear and remains colorless when acetic acid, alcohol and hydrogen peroxide are added to a portion of it in a test-tube. The solution is stable for several weeks. In the course of time oxidation of the phenolphthalin around the lip of the bottle may occur. It is always advisable to use a colorless solution. The method of performing the test Boas describes as follows: An acetic acid-alcohol extract (5 gtt. acetic acid and 15-20 c.c. alcohol) of the feces is prepared. From a dropping bottle 15 gtt. of the reagent are placed in a test-tube, to which are added 5-6 gtt. of 3 per cent. hydrogen peroxide and 2 c.c. of absolute alcohol. The tube is well shaken. The fecal extract is filtered and the filtrate is allowed to run slowly into the test-tube, so that it forms a layer with the prepared reagent, about one-half of the filtrate being employed. If blood coloring matter is present, there appears immediately or gradually a rose or deep red ring at the line of contact, the depth of color depending upon the amount of blood pigment present. If the color is faint, it is more readily perceived by placing the tube before a white background. The result of the test is rarely doubtful. But when such is the case, Boas proceeds in the manner devised by Schumm for increasing the delicacy of the guaiac test; the feces are rubbed up with equal parts of alcohol and ether, filtered repeatedly, and then the filtrate is evaporated to dryness. The dry residue is suspended in acetic acid-alcohol and filtered. Then, using the filtrate as the fecal extract, the method as described above is followed, when the rose-colored ring becomes definite if blood is present. Boas has carried out duplicate tests with guaiac and with benzidin. He has found the phenolphthalin test more delicate than the benzidin and much more sensitive than the guaiac. Furthermore, whenever he has found the guaiac and benzidin tests positive, the phenolphthalin test has always been plainly positive. The observations described above relate only to occult blood in the feces. With stomach contents the contents are different, and will be discussed in a subsequent communication.

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**Observations on Infection and Immunity in Maternal and Fetal Lues.**—From his observations on large material of his own and from reports in the literature, J. TRINCHESE (*Deutsch. med. Wchnsch.*, 1915, xli, 555) has reached certain definite conclusions in regard to luetic mothers and their offspring, which he summarizes as follows: I. Colles' law is false, *i. e.*, an immunization of the mother by the fetus is impossible, because (a) a paternal infection of the fetus does not occur and (b) the fetus produces no immune bodies. II. Profeta's law is misleading. Immunization of the fetus by the mother does not occur, for the placenta is impermeable to the immune bodies of the maternal organism. III. The earlier the fetus is infected, the more rapidly the syphilis advances after the manner of sepsis, which leads to the death of the fetus within six weeks. IV. Until about the eighth month the fetus forms no immune bodies and its blood is therefore negative to the Wasserman reaction, though its tissues may be swarming with spirochetes and the mother's blood may yield a positive

Wassermann reaction. V. In the last month of pregnancy the fetus begins to develop protective substances and its blood may give a positive Wassermann test. VI. If the infection of the child occurs in the last few weeks before birth, clinical symptoms of lues at birth may fail and the Wassermann reaction may be negative, since the incubation period for both phenomena may have been too short. These are the children formerly looked upon as immune. They are, in reality, the "late" syphilitic children. VII. If, indeed, it happens that latent or even florid luetic mothers bear healthy children, then, in consequence of VI neither the lack of symptoms nor the negative Wassermann reaction is certain evidence that the child is healthy. VIII. The following are the possibilities at birth for the offspring of syphilitic mothers: 1. The child is clinically syphilis-free and has a negative Wassermann reaction. 2. The child is clinically syphilis-free and has a positive Wassermann reaction. 3. The child has clinical syphilis and a positive Wassermann reaction. 4. The child has clinical syphilis and a negative Wassermann reaction. In the sequence given, the possibilities for the life of the child become progressively worse, so that the fourth generally means the death of the child.

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**Vaccination Against Typhoid in the United States Army.**—LYSTER (*Jour. Amer. Med. Assn.*, 1915, lxy, 510) says that for the decade 1900 to 1909 there were 3,510 cases of typhoid fever among the American troops, with an average therefore of 351 cases per annum. In 1909 up to September 1, 830 individuals had received one or more doses of the typhoid vaccine, a number which, for all practical purposes can be disregarded. In this year there were 282 cases of typhoid in the army consisting of a mean strength of 84,077. In the year 1910, 16,093 persons were vaccinated. One hundred and ninety-eight cases of typhoid are reported for the same year. In 1911 from January to June 30, nearly 28,000 officers and men were vaccinated. The routine vaccination of all recruits was begun in June, 1911, and on September 30, 1911, vaccination was made compulsory for the entire army. The gradual introduction of vaccination against typhoid began to show results as soon as it was done on a scale of any size. This was by the end of 1910. In that year, with 198 cases of typhoid fever, it can hardly be stated that the disease was "practically abolished" by improved sanitation, as the antivaccinationists would have us believe. By the end of 1911, seventy cases of typhoid fever had occurred. By the end of the first quarter of 1912, practically all of the army was vaccinated, and new men coming into the service were being vaccinated as soon as enlisted. There were twenty-seven cases to the end of that year and nineteen of these were in the persons of soldiers who had not been vaccinated against typhoid fever. When vaccination can be said to have become complete, as in 1913 and 1914, there were four and seven cases, respectively, and only two of these had had the complete course of vaccination when they were taken with typhoid fever. The standard of sanitation maintained has not varied noticeably for some years. The only change in recent years has been a system of conservancy in camps that largely prevents flies entering the latrines and becoming conveyors of disease. But this could have affected only a small part of our troops in any year. In

1911 from 10,000 to 12,000 out of a total of 92,802 were in camps; during the last two years (1913-1914), from 12,000 to 15,000 out of a total of 92,580. Finally it must be remembered that the soldier comes into quite as intimate contact with civilians as he does with his comrades. He contracts diseases (measles, mumps, scarlet fever, influenza and others) just as he did before, with the exception of smallpox and typhoid fever. Why are these diseases practically no longer existent among our soldiers? Vaccination against smallpox and against typhoid fever are the active agents in banishing these diseases from armies that thoroughly and efficiently use these measures. It may be of interest to add that for the first six months of 1915, only one case of typhoid has so far been reported as occurring in the United States Army.

## SURGERY

UNDER THE CHARGE OF

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**Gastrostomy for Stomach Drainage.**—NYSTRÖM (*Zentralbl. f. Chir.*, 1915, xl, 721) says that Jaboulay, in 1905, employed the stomach fistula in a case of peritonitis with ileus to control the great distention of the abdomen and obtained a marked relief of the respiratory disturbance. The patient recovered. It has been employed with success in cases of volvulus of the small intestine and gastric dilatation. The direct permanent drainage of the stomach by gastrostomy is indicated especially in two kinds of cases: (1) In ileus. Through stomach drainage the intestinal contents streaming into the stomach are immediately and continuously being evacuated. The distention of the upper part of the abdomen is removed, the diaphragm can move more freely and the heart action and respiration do not suffer as when the diaphragm is forced upward. Vomiting ceases and the patient drinks freely without evil consequences. (2) In operations on the stomach, this procedure is indicated when a suture insufficiently cannot be avoided, and when a pre-operative or operative obstruction cannot be overcome by an anastomosis operation at the same sitting. It is especially valuable in operation for a perforated gastric or duodenal ulcer with peritonitis, or in intestinal paresis. It removes the toxic intestinal contents from the stomach, and the distention of the upper part of the abdomen, and thereby protects, from internal pressure, the ulcer often sutured

with difficulty. Any operation necessary for an existing stenosis may be postponed until a later, more favorable, time. The gastrostomy is best performed according to the technic of Witzel. The aseptic introduction of a soft catheter will be rendered easy through a suitable canula. A purse-string suture is first introduced, including about a square centimeter of the anterior wall of the stomach. This portion of the stomach is seized on both sides by tooth forceps and held up, when it is penetrated within the suture circle by the canula armed with the soft catheter. A small incision through the serous and muscular layers makes this more easy. The canula is then withdrawn and the catheter allowed to remain. The purse-string suture is then tied, the catheter invaginated a few centimeters and held there by a chromic catgut invagination suture. Nyström does not fix the stomach to the abdominal wall, but allows it to remain completely free and the catheter to pass between the sutures of the abdominal wall, the wound in which is completely closed in the usual manner. After about two weeks the catheter is usually loose and may then be removed if all is going well.

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**A Review of the Literature of Fractures.**—HUNTINGTON (*Ann. Surg.*, 1915, lxii, 264) from a comprehensive survey of the literature concludes that the public demands, and is entitled to, better results from fracture treatment than have, hitherto, been obtained; that from 80 to 90 per cent. of long bone fractures can be successfully treated by the closed method; that conservative treatment exacts a high degree of skill and close attention to details; that resort to the open method is of too frequent occurrence; that the least possible amount of foreign fixation material should be the rule; that steel plates, in the treatment of fractures, are a menace from the standpoint of permanency; that the bone implant is the fixation material of choice; that intramedullary splints are inferior to the autogenous bone implant; that fixation material of whatever type is not to be relied upon for maintenance of alignment; that cases of non-union and faulty union which come to secondary operation indicate indifferent methods of primary treatment; that operative treatment of compound fractures should be withheld until the external wound healing is perfected; that many joint fractures can only be treated successfully by the open method; and that normal contour and good function are closely related in end-results of all fractures.

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**Banti's Disease.**—KRULL (*Mitt. u. d. Grenzgeb. d. Med. u. Chir.*, 1915, xxviii, 718) says that the so-called Banti's disease is an unusual form of the so-called atrophic cirrhosis of Laennec. This deviation consists in the unusual size of the splenic enlargement and in the clinically more or less strong protuberance. The frequent occurrence of vomiting of blood accounts for the high-grade anemia. As in liver cirrhosis, it is often impossible to discover a cause. At times, however, a preceding condition can be held accountable, as syphilis, congenital or acquired, malaria or gastric disturbances. The weight of the spleen as given by Banti (1000 to 1500 gm.) is much too low. It is better not to fix the weight definitely, since it has been repeatedly shown that the splenic swelling is not proportionate to the weight. A so-called Banti's spleen is described as follows: The normal shape is preserved, the capsule is

thickened, the consistency increased, and the parenchyma is usually of a dark red color, but sometimes is brighter red. The pulp and Malpighian corpuscles are the seat of a more or less advanced sclerosis. With regard to the anemia which all investigators, almost without exception, have established by inspection; one is surprised to find that the red blood corpuscles are not much below normal, as one is inclined to expect. Cases with 4,000,000 red blood corpuscles have been repeatedly reported. This contradiction finds its explanation, aside from the fact that inspection alone cannot be depended for the diagnosis of an anemia, in the greater reduction of the hemoglobin than of the red blood corpuscles. Leukopenia is also present in this condition. In connection with the liver, the other chief organ involved in Banti's disease, Krull says: The connective tissue is increased. The surface is rough and irregular, but the organ is not necessarily always contracted. Ascites may occur; jaundice, when present, is slight. Besides nosebleeding, which Banti mentioned, gastric hemorrhages occur repeatedly in the course of the affection.

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**Operative Treatment of Tumors of the Bladder.**—GARDNER (*Ann. Surg.*, 1915, lxii, 456) says that the results of operation on tumors of the bladder during the past fifteen years, as presented in his paper, were gathered through the old method of sending blanks to a number of the leading urologists, asking for answers to specified questions. In this way the records of 369 cases have been procured (Watson's report of 1160 cases, including Beer's 183 cases treated by high-frequency current, Oudin, has been taken as the basis of this report). Since publishing his report and within the past five years Beer has seen 59 additional cases. Judd's report of 114 cases at the Mayo Clinic is also included, which makes the total 1702. He concludes that: In the treatment of carcinoma the transperitoneal method as used in the Mayo Clinic or the subtotal cystectomy of Squier, with wider resection of the bladder wall, offers the best method. These methods give the operator opportunity to look for enlarged glands or metastases and if necessary the ureters can be easily transplanted. Cystotomy and excision and actual cautery should only be used in terminal cases as a palliative method to relieve pain and hemorrhage. When the growth involves both ureters Watson's operation of total cystectomy with a primary operation for transplanting the ureters into the loin shows the best results. In the treatment of papilloma, intravesical high-frequency current, during the short time it has been used, has given better results than any other method, reserving the question for time and statistics to determine whether this method by reason of the difficulty in distinguishing between papilloma and carcinoma is shown to be as satisfactory as wide resection, such as is advised for carcinoma.

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**Errors in Diagnosis of Renal and Ureteral Calculus.**—CABOT (*Surg., Gynec. and Obstet.*, 1915, xxi, 403) says that in a recently undertaken study of 153 cases of stone in the kidney and ureter at the Massachusetts General Hospital, it was noted that 26 abdominal operations had been done upon these patients without relief of the symptoms, which were clearly due to the overlooked calculus in kidney or ureter. The appendix was the most frequent sufferer and was removed in 10 cases

without benefit. What are described as exploratory laparotomies came next in frequency, with 8 cases. Fixations of a kidney supposed to be movable and producing symptoms followed in order with 4. Then came removal of tube and ovary, unsuccessful search for gall-stones, an attempt to relieve adhesions, which did not exist, stripping of the capsule of the kidney for nephralgia, and as a crowning iniquity, suprapubic cystotomy on a normal bladder for a stone which was seated some two feet away. Cabot lays down the following rules as likely to avoid these errors if carefully followed: In all cases of abdominal pain of a chronic or recurring type, in cases of backache, lumbar or sacro-iliac joint strain and lumbago, careful repeated examinations of the urine, including a microscopic examination of the sediment in all cases whether albumin is present or not, and of a catheter specimen in all female patients, should precede positive diagnosis. In most of these cases in which the symptoms warrant the consideration of operation, roentgen-ray plates are essential. The evidence presented by the roentgen-ray alone is insufficient to warrant operation in most cases of stone in the kidney or ureter. Possibility of error by mistaking other foreign bodies should be excluded by the use of the ureter catheter, stereoscopic plates, injected roentgenograph, or the waxed tip catheter. In any case in which the symptoms suggest ureteral calculus and a doubtful shadow appears in the roentgen-ray plate, if the ureter cannot be catheterized on repeated attempts or the catheter is arrested at the same point on various occasions, the decision for or against operation must be made upon the apparent gravity of the symptoms. In cases with symptoms suggesting stone in the kidney, with a normal urine, a negative roentgen-ray, and an unobstructed ureter, the wax-tipped catheter will not infrequently lead to a correct diagnosis and will be likely to fail only in the cases in which the stone lies in a dilated calix and is therefore out of reach of the catheter.

**Shock and Hemorrhage: An Experimental Study.**—MANN (*Surg., Gynec. and Obstet.*, 1915, xxi, 430) says that the problem at hand was to determine whether there is in shock an actual loss of circulating blood and, if so, whether the loss can be accounted for by vasomotor failure. The amount of blood that can be obtained from a large arterial trunk—as the femoral—is the measure of efficient blood; it is the amount which can be returned to the heart and lungs and, after aeration, be pumped out to feed the tissues. The blood which can be secured from the venous side of the circulatory system—as from the right auricle—is the amount that is freely movable but was not returned to the arterial system. Their sum is the amount of mobile blood in the body. This sum subtracted from the total amount of blood gives the quantity of immobilized blood; the fixed quantity in the tissues. So far as the immediate circulatory needs of the organism are concerned, this latter amount of blood is useless. He summarizes his experiments as follows: In a normal dog 66 per cent. of the blood can be obtained from the femoral artery and 10 per cent. from the heart, making a total of 76 per cent. which can be secured, leaving 24 per cent. in the tissues. In an animal in which the cervical cord is sectioned, producing medullary vasomotor paralysis, 54 per cent. of the blood can be obtained from the femoral artery and 12 per cent. from the heart, a total of 66 per cent.,



leaving 34 per cent. in the tissues. In an animal in which blood-pressure is depressed practically to zero by an overdose of ether, 46 per cent. of the blood can be obtained from the femoral artery and 13 per cent. from the heart, making a total of 59 per cent., leaving 41 per cent. in the tissues. In an animal in which the viscera have been exposed until the clinical signs of shock are present but in which the vasomotor reflexes are as active or even more so than in the normal condition, only 28 per cent. of the blood can be obtained from the femoral artery and 11 per cent. from the heart, making a total of 39 per cent., leaving 61 per cent. in the tissues. He concludes that: The clinical signs of shock which appear after section of the abdomen and exposure of the viscera are due to a loss of circulatory fluid. This loss of fluid is not dependent upon any primary impairment of the medullary vasomotor centre and takes place at a point beyond the control of the vasomotor mechanism. The causes for this loss of fluid are apparently the same as those which determine the accumulation of fluid in any irritated area and produce the signs of inflammation. The nervous system probably plays no greater part in the former case than in the latter. The condition is made grave when the viscera are exposed because of the great vascularity of the tissues involved.

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**A Radical Operation for Hemorrhoids by a Simple Suture.**—TILLMANN (*Zentralbl. f. Chir.*, 1915, xlii, 737) describes his operation as follows: According to the size, character (pedunculated or not) and number of the hemorrhoids, the local anesthesia will be produced either by a simple injection under the nodes or by a circular injection of the anus. Deep analgesia of the internal and external sphincters by the latter method will be necessary for the stretching of the sphincter and will require a 1 per cent. novocain in solution. For the more superficial injection a 0.5 per cent. solution will be sufficient. Each hemorrhoid is pulled outward by a forceps and then grasped in a radiating direction by a suitable clamp. A catgut suture is used to complete the operation. The needle is passed through the pile at the anal end of the clamp and under it. It is tied and the free end left long. Then it is continued to the other end of the pile as a continuous mattress suture. This portion of the suture serves as a protection against hemorrhage and at this point it is permitted to hang aside unknotted. Now the pile is cut away close to the clamp and the clamp removed. The suture is again used to bring the wound edges into close apposition, and when this is completed the two free ends will be together again at the anal end of the pile where they are tied together. The separate nodules or piles are treated in the same way. The special advantages of the operation are; its bloodlessness, the exact union of the wound edges, and therefore the diminished risk of infection, the rapidity with which the operation can be completed and its simplicity. In the first year of the war 40 cases were thus treated. The average time after operation before the soldier was ready for service was 14.7 days.

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**Eckehorn's Operation for Prolapsus Ani in Adults.**—BECKER (*Zentralbl. f. Chir.*, 1915, xlii, 772) says that prolapse occurs in war time, usually from long-continued diarrhea, and may be so troublesome that the soldier is unfit for service. In 1 case the prolapse was 3 cm.

long, bled freely, was ulcerated and difficult to reduce because of the swelling, and recurred after every defecation. Under local anesthesia on both sides of the coccyx, a long pedicle needle is introduced first on one side of the coccyx. Two fingers in the anus hold up the prolapse. Under the guidance of the finger the needle is pushed on under the mucous membrane to a point opposite its entrance and made to emerge at the junction of the skin and mucous membrane. The end of the suture is then held and the needle withdrawn. On the other side of the coccyx, the needle not armed with the suture is again introduced in the same manner as before and made to emerge again at the same point near the junction of the skin and mucous membrane. The free end of the suture is threaded into the needle and both withdrawn through the last needle canal. While two fingers hold back the prolapse, the two free ends of the suture coming out on the two sides of the coccyx are tied together over a tampon. Moderate diet is given for three days, and 20 drops of tincture of opium 3 times daily. The first stool should occur five days after the operation. The suture remains twenty days, and during that time is frequently tightened over a new tampon. There has been no recurrence of the prolapse after three-quarters of a year.

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**Gastric Fistula with Suction Drainage for Atonic Conditions of the Stomach and Intestine.**—GROSS (*Zentralbl. f. Chir.*, 1915, xlii, 785) refers to Nyström's recent article on gastrostomy for stomach drainage (abstracted *Progress of Surgery*, page 285). He has had an experience with over 200 cases, and during 1913 and 1914 made a special study of 47 cases. Since then he has used the suction drainage in 33 new cases and has established its great value. It guarantees in atonic conditions of the stomach and intestines, a continuous evacuation of the retarded contents and permits at the same time an immediate introduction of suitable quantities of fluids from the mouth. On the basis of his material, Gross considers it an important aid to operation in (1) peritonitis, even in the beginning when there is only threatened atony; (2) ileus, as soon as frequent vomiting sets in and distention of the stomach occurs or is anticipated; (3) acute dilatation of the stomach; (4) infections or other affections of the upper and middle abdominal regions which cause a gastric disturbance or make its early occurrence probable; (5) perforation of a gastric or duodenal ulcer, after the perforation has been attended to. He employs the old method of performing simple gastrostomy. A small area of the stomach surface is attached to the abdominal wall by a few sutures and is opened between two forceps, wide enough to permit the introduction of a firm rubber tube 5 to 8 cm. into the stomach. A glass tube union between this and another longer rubber tube passing into a vessel on the floor, provides for control of the current by the eyes and for suction drainage. Gross objects to the use of so small a tube as a No. 14 to 18 Nélaton catheter. With the associated complete paralysis of the intestines and the antiperistaltic stream which keeps the pylorus open, he thinks it impossible for so small a tube to carry off the fecal masses that are present. In other respects he regards Nyström's contribution as a very valuable one, since it promotes the idea of the necessity for the continued evacuation of the stomach in atony of the stomach and intestines.

## THERAPEUTICS

UNDER THE CHARGE OF

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**Is There a Successful Treatment of Scarlet Fever.**—Koch (*Deutsch. med. Wchnschr.*, 1915, xli, 372) says that during a period of ten years the mortality of 1438 cases of scarlet fever treated by Barasch on the ordinary plans of treatment was 15 per cent. He compares this with his own mortality of 1.1 per cent. in 263 cases and ascribes the discrepancy entirely to his systematic use of serum therapy. The course of scarlet fever during the period embodied in this report of Koch's was not milder than usual, rather the reverse, for a larger proportion than normal were of a more severe type. Koch advocates strongly the intravenous injection of large quantities, at least 100 c.c., of serum taken from patients convalescent from scarlet fever. In the statistics of Barasch, Koch points out as noteworthy the fact that the majority of the patients died during the early stages of the disease and the minority died later from various complications. This is an important point for it is during the early stages in particular that serotherapy is most efficacious. Koch regards it as almost specific during this stage and says that the prompt effects seen in this connection far surpass those of autotoxin in diphtheria. Normal serum also is of distinct therapeutic value but the serum of convalescent patients is more powerful. It is also of distinct advantage to use the mixed serum obtained from several convalescent patients. He warns against the subcutaneous method of giving the serum, and inadequate dosage. The serum should be sterilized before injection and it can be kept in ampoules after sterilization and the addition of 0.5 per cent. of a 4 per cent. solution of phenol. The dose should be at least 50 c.c. for young children and 100 c.c. for older ones.

**Intravenous Iodid Therapy.**—KLEMPERER (*Therap. d. Gegenw.*, 1915, lvi, 85) writes concerning the intravenous use of sodium iodid. The author has given over one hundred such injections and has never had any untoward results from its use. He advocates the intravenous use of sodium iodid in doses of from 5 to 20 grams, two or three times a week, especially for the treatment of syphilis where a marked iodid action is desired in as short a time as possible. Among the syphilitic affections especially benefited by such intravenous iodid medication, he mentions syphilis of the central nervous system, tabes, syphilis of the circulatory system and of the liver. Klemperer recommends this treatment particularly for syphilitic aortitis to be used in combination with salvarsan therapy. His practice is to give a small dose of salvarsan from 0.1 to 0.2 grams followed immediately by the intravenous administration of from 5 to 10 grams of sodium iodid in a 10

per cent. solution. The intravenous use of sodium iodid, however, should not be confined to the treatment of syphilis but is recommended for any condition where an iodid medication is not well borne by mouth. Klenpferer has never seen any serious untoward effects from intravenous iodid medication even in doses as high as 40 or 50 grams. Occasionally some of the minor symptoms of iodism develop such as conjunctivitis and a slight but transient headache. He has seen cases where iodid medication by mouth was not tolerated but well borne when given intravenously. The injections are absolutely painless and technically easy to perform. Examination of the urine has shown that the iodid is not excreted as rapidly when given intravenously as when given by mouth.

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**Report on the Allen Treatment of Diabetes.**—HILL and SHERRICK (*Boston Med. and Surg. Jour.*, 1915, clxxii, 696) report a very successful series of cases of diabetes treated by the method advocated by Allen. They found that this treatment is simple, safe and very efficacious in rendering and keeping a patient sugar-free, in a much shorter time than was possible by the old method. Their method of treatment was as follows: As soon as the patient enters the ward he is put on house diet without extra bread or potatoes and kept on this for two days to determine his tolerance for ordinary diet and the severity of the diabetes. On the third day he is put to bed and given nothing but black coffee with one ounce of whiskey every two hours from 7 A.M. to 7 P.M., seven ounces of whiskey in all, representing about 800 calories. If there is much acidosis, as indicated by the amount of diacetic acid and acetone in the urine, sodium bicarbonate is given, otherwise not. The patient is kept on this regime until he is sugar-free; in most of the cases it took either two and a half or three days to accomplish this. The loss of weight is very slight; the relief of symptoms, such as pruritus polydipsia, etc., is very striking and they have never seen any indication of acid poisoning in the cases treated by this method. As soon as the patient is sugar-free, he is given "a vegetable-day," i. e., vegetables containing not over 5 per cent. of carbohydrates, boiled twice, with a carbohydrate content of about 15 grams after boiling. After a single vegetable day the diet is changed to one containing a carbohydrate content of 15 grams, a protein content of 25 grams and a fat content of 150 grams. From this the diet is slowly raised, increasing first the fat, then the protein, and lastly the carbohydrate. The fat is never raised above 200 grams and the calories seldom above 2,200. On this the patients hold their weight, feel well and usually remain sugar-free. The series of cases reported by the authors is small and details of the cases are included in the article. In no case did they have any unfortunate results—never any sign of coma. In every case the patient has become sugar-free and has stayed so, on a reasonable diet which enabled him to hold his weight. Some of the cases treated were severe cases of diabetes, young people, whom they had treated before by the old method and could not get sugar-free.

**Clinical Studies in Caffein.** TAYLOR (*Arch. Int. Med.*, 1914, xiv, 769) reports his observations that were undertaken to test the effect of caffein on the pathological circulatory system of the human being.

He says that results obtained experimentally by intravenous injection of caffeine in animals are in no way comparable with results when the drug is given to human beings by mouth, in the usual clinical way, where the absorption is more or less delayed and in cases in which the cardiovascular system is not intact. These observations were made on fifteen patients suffering from advanced myocardial disease. Every case showed some sign of broken compensation at the time of the experiment and thirteen gave evidence of retained body fluid. Dyspnea was present in 14 cases; edema of the extremities in 13 cases; ascites in 10 cases; hydropericardium and hydrothorax, single or double, in 6 cases; tender pulsating liver in 6 cases. Other common symptoms were cough, frontal headache, weakness, dizziness, and sub-sternal pain. All patients were reported in bed on a constant diet. Taylor notes in detail the effects observed upon the pulse rate, respiratory rate, blood-pressure, diuresis, and body weight. He sums up the clinical efficiency of caffeine saying that the results were excellent in eight cases. Moderate in four, and no favorable effect was obtained in three. In one of the cases in which there was no result the vomiting and loss of sleep even on small doses more than balanced any possible good that the drug could have done. All the cases with limited results showed the nervous signs, so the absorption of the drug was assured. Unpleasant symptoms, mainly nervous and gastric, occurred in thirteen of the fifteen patients. The doses used were full doses but when they were reduced below the point where they gave nervous phenomena their cardiac value had disappeared. In five of these cases a second admission to the hospital on a return of symptoms while they were still in the institution made it possible to try the comparative therapy of theobromin sodium salicylate under the same conditions and on the same heart on which the caffeine action had been tested. Its action on the urinary outflow is more prompt than that of caffeine and the diuresis is larger. One can usually tell in twenty-four hours, in a given case, whether theobromin sodium salicylate will act or not; while with caffeine the third or fourth day is more apt to show results. The theobromin sodium salicylate action is equally well sustained and usually at a higher level than the caffeine. Where caffeine has a depressing effect on the vasomotor system and lowers the blood-pressure, theobromin sodium salicylate first elevates the pressure and then later lowers it. Taylor regards 80 grains a day as a normal clinical dose. Patients will tolerate this dose easily. Not only was the theobromin sodium salicylate action prompter, much stronger and equally well sustained but it also did not show the gastric and nerve disturbances attendant on caffeine. Taylor in his summary says that in myocardial insufficiency with retained body fluid, caffeine causes a moderate increase in the urine output with a proportional loss of body weight. This increase reaches its maximum on the fourth day; a drop in both the systolic and diastolic blood-pressure which may stand in a causal relation to the diuretic coefficient, contrary to the usual teaching; a slight (3.6 per cent.) temporary rise in the pulse-rate, but no permanent change in either the pulse or respiratory rate; a moderate relief of the cardiac symptoms; the constant appearance of distressing nervous and gastric symptoms. He believes that the clinical diuretic action of caffeine may be better performed by large doses of theobromin sodium salicylate without the unpleasant side effects.

**Emetin Hydrochloride.**—ROBINSON (*Practitioner*, 1915, xev, 544) has had very good results with the use of emetin hydrochloride for the treatment of pulmonary hemorrhage occurring in pulmonary tuberculosis. In mild cases, he gives a dose of two-thirds of a grain daily and continues its use for five days after the sputum has become free of blood. He has found that emetin hydrochloride has been uniformly successful in checking the hemorrhage in about three days. Similar results were obtained in controlling hemorrhage from gastric ulcer by Robinson. He cites a severe case of mucous colitis associated with dysmenorrhea, who was much benefited by emetin hydrochloride and hopes that others may be led to try the same treatment for similar conditions. Robinson has found that the sole drawback to the use of emetin hydrochloride is that there is a certain amount of local tenderness after subcutaneous or intramuscular injections. This, however, is not sufficient to prevent its daily administration for long periods.

**Specific Treatment in Typhoid Fever.**—GAY (*Jour. Lab. and Clin. Med.*, 1915, i, 13) summarizes the history of the specific treatment of typhoid fever. The first twenty years experience since 1893 with the use of ordinary preparation of typhoid vaccines administered subcutaneously gave some encouragement for the method in the matter of symptomatic improvement, shortening of the duration of the disease, decrease of the mortality, lessening of relapses and complications, with a few abortive cures. The results obtained were of doubtful value and inspired little confidence that the true specific treatment had been found. Modern investigations have introduced the intravenous administration of dead or living cultures and particularly of sensitized cultures of the typhoid bacillus. With such methods far more striking results have been realized. Abortive cures occur in a considerable percentage of cases, perhaps in as high as 30 to 40 per cent. If one working hypothesis is correct, these abortive cures are due to the presence of antibodies in a patient who is actively combating the disease, and cure is affected by the action of these antibodies on the circulating bacteria, combined with a specific hyperleucocytosis produced by the vaccine, particularly when it is specific and sensitized. The remaining cases might possibly be favorably affected by a combination treatment of sensitized vaccine and a suitable immune serum which would supply the lacking antibodies.

**Concerning Exercise in the Treatment of Severe Diabetes.**—ALLEN (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 743) says that tests were made first in diabetic dogs, with a known constant limit of tolerance for carbohydrate or protein. It was found vigorous exercise markedly raised the tolerance of such animals, as judged by the sugar in both urine and blood. In some experiments, dogs which for months past had regularly shown glycosuria whenever they were given 100 grams of bread, on exercise were able to take 200 grams of bread as a regular daily ration without glycosuria. The tests with patients are more recent, but the results thus far appear sufficiently favorable to warrant recommending exercise as an addition to the treatment of diabetes. Some of the severest cases are too weak for exercise at first, but it is begun as early in the period of dieting as practicable and generally

the weak patient is able to do more than he or his physician supposed. In suitable cases the blood-sugar may be found to fall rapidly during a half hour or hour of lively exercise. In the earlier or more severe cases, it may rise thereafter; but often it will continue to fall after the exercise has ended, and remain for sometime at a lower level. In a patient free from glycosuria with persistent hyperglycemia, one fast day with exercise may reduce the blood sugar so much as several fast days without exercise. Allen says that it is hoped that this addition to the treatment of severe diabetes will prove of special value to children, to patients with persistently low tolerance, and perhaps to some of that class previously so hopeless, namely, tuberculous diabetics. For the ordinary type of patients it may be a means of getting results somewhat more quickly and thoroughly, and leading to a higher degree of both comfort and usefulness. The value of exercise is strictly limited. It cannot raise tolerance very high, and it is not equal to the dietary regime in importance. Results will be unfortunate if it is used merely as a means for shortening the hospital care of the patient or for building up weight and strength at the cost of more important considerations. The radical and permanent control of the diabetes is the essential matter, and is to be judged by such things as glycosuria, acidosis, and blood sugar, not by a temporary sense of well-being. A stern program of fasting, low diet, and reduction of weight is still necessary as before, but it is hoped that results may be more beneficial with the use of exercise as an additional detail of the treatment.

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**Poisoning by Mercuric Chlorid and its Treatment.**—LAMBERT and PATTERSON (*Arch. Int. Med.*, 1915, xvi, 865) report very good results with the following treatment for acute mercuric chlorid poisoning: The first indication is to give the patient the whites of several eggs and then to wash out the stomach thoroughly. This has usually been done before the patients are admitted to the hospital. On admission, the stomach contents are expressed and examined for mercury, the stomach is thoroughly washed, and a pint of milk introduced. If no stomach contents are obtained before lavage, then the lavage water is examined for mercury. Urine passed spontaneously, or that obtained by catheter, is examined for mercury. The metal appears in the urine in from three to twenty-four hours after it has been swallowed. If more than a day has elapsed since the poisoning occurred, a stool should also be examined for the poison. If the first lavage does not allay the nausea and vomiting, it is repeated after an hour, and the following routine is begun as soon as the stomach will permit: (1) The patient is given every other hour 8 ounces of the following mixture: potassium bitartrate, 1 dram; sugar, 1 dram; lactose, one-half ounce; lemon juice, 1 ounce; boiled water, 16 ounces. Eight ounces of milk are administered every alternate hour. (2) The drop method of rectal irrigation with a solution of potassium acetate, a dram to a pint, is given continuously. The amounts of urine secreted under this treatment are very large. (3) The stomach is washed out twice daily. (4) The colon is irrigated twice daily, in order to wash out whatever poison has been eliminated in that way. (5) The patient is given a daily sweat in a hot pack. The authors emphasize the necessity of keeping up the treatment with the colonic drip enteroclysis day and

night without interruption. In cases in which one single dose has been taken, after two negative examinations of the urine, on successive days, it seems legitimate to stop the treatment. For the less severe cases, a week may be a sufficient time for treatment. When large or successive doses have been taken, or when there is a preëxisting kidney lesion, or when treatment begins several days after the poison is taken, longer periods of treatment, up to three weeks, are necessary. Under the treatment detailed above, these patients quiet down to their routine and, as a rule, do not suffer except from the discomforts of the therapeutic measures. The stomach becomes tolerant of the milk diet and the alkaline drink after from twenty-four to thirty-six hours. The kidney secretion at first is excessive, and may run up to 130 or more ounces in the twenty-four hours. This usually diminishes in spite of the continued exhibition of fluid between the fifth to the tenth day, and may nearly stop altogether. It is at this period that the continuous water cure and the rest in bed must be insisted on. If this period is successfully passed, the secretion of urine again increases often to a higher level than at first. The mercury itself seems to act as a diuretic at this stage of the treatment. The bowels usually show some irritation, but when the treatment is faithfully carried out, the tendency to diarrhea and colitis is regularly controlled by the colonic irrigations, and other medication for this symptom has been rarely necessary.

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**Coagulen in the Treatment of Pulmonary Hemorrhage.**—RIEDL (*Wien. klin. Wchnschr.*, 1915, xxviii, 7) advises the use of coagulen to control pulmonary hemorrhage. Coagulen is prepared from the blood platelets of animals. It is a yellow powder, soluble in water and its solutions can be sterilized without destroying its efficacy. The theory of its action is that the blood platelets are supposed to contain the thrombozyme which unites with the thrombogen of the blood plasma and, in the presence of calcium salts, causing clotting of the blood. Coagulen has been used as a local hemostatic in operations and Riedl advocates its use hypodermically and intravenously in internal bleeding. He believes it is effectual to control bleeding in hemophilia and other hemorrhagic diathesis. When used intravenously solutions in the proportion of 1 gram of coagulen to 40 c.c. of distilled water are used after sterilization by boiling for a few minutes. Riedl has had success in the treatment of pulmonary hemorrhages with such injections and advocates the more general use of this remedy for that purpose.

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**A Study of Different Nitrogenous Diets in Chronic Nephritis.**—FROTHINGHAM and SMILLIE (*Arch. Int. Med.*, 1915, xv, 204) believe that it is justifiable to conclude from their study that in certain types of chronic nephritis the nitrogenous content of the diet should be carefully watched in order to prevent an increase in non-protein nitrogen in the blood. The exact effect of an increase in blood nitrogen produced by a high nitrogenous diet is not known at present, but presumably it is unfavorable to the best interests of the patient, since in some it increases their discomfort. A diet low in nitrogen content will frequently keep down to normal the non-protein nitrogen of the blood in chronic nephritis.



## PEDIATRICS

UNDER THE CHARGE OF

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**Treatment of Infantile Beriberi.**—JOSÉ ALBERT (*China Med. Jour.*, 1915, xxix, 381), in an interesting article on infantile beriberi, holds this to be the most interesting problem of pediatrics and of general medicine in the Philippine Islands. It is without parallel elsewhere, since the infant mortality among breast-fed children is greater than that among the artificially fed. Among children under one year 38 per cent. are victims of the disease. Hirota, of Japan, has established that infantile beriberi is a true intoxication from ingesting beriberic milk, and that the discontinuance of maternal feeding is the only and safe means of cure which occurs during the first week of the procedure. The substitution of artificial feeding being extremely difficult and usually dangerous among the class of people affected. Bréaudat, Gabriel and Guerrero fed the mothers of beriberic infants with rice polishings (tiqui-tiqui) and mango—two antiberiberic foodstuffs. Owing to the unpalatability of this food and the necessity of employing artificial feeding for a certain length of time, the method did not spread. Chamberlain and Vedder of the U. S. Army Board advocated the use of the extract of tiqui-tiqui without the discontinuance of maternal feeding. Five cubic centimeters of the extract represent 82 grams of rice polishings. The dose is 5 c.c. a day given in 20-drop doses every two hours while the child is awake. The use of this extract, if given in time and in sufficient doses, is followed by immediate and marked improvement, the clinical syndromes change in twenty-four hours, and in three days the disease has disappeared with the exception of the aphonia, which lasts for seven or eight weeks. Treatment should be continued as long as aphonia persists. In stubborn cases the dose should be increased. In cases without aphonia treatment should be continued at least three weeks after apparent cure. Failure of the extract to effect a cure may be due to extreme severity or advanced neuritis, cases associated with other infections such as bronchopneumonia, and deficiency of the active principle in the extract. The extract is a vagotropic drug, supplying vitamins to the vagus nerve.

**Serum Treatment of Scarlet Fever.**—EMIL REISS and JOHANNA HERTZ (*München. med. Wchnschr.*, 1915, xlii, 1177) report further observations on the treatment of scarlet fever with convalescent serum. They have come to the use of this form of treatment almost routinely instead of using it only in the most toxic cases with poor prognosis. In one year 33 children were treated by the serum method out of 413 cases of scarlet fever admitted. The 33 cases included only acute, toxic cases with doubtful or poor prognosis. Of this number

but 1 died of the fulminating type of fever and 2 others died from subsequent intercurrent conditions. Most of the treatments were given during the first five days of the disease. Convalescent serum was used in this series, and the most significant factor in the result was the marked improvement in the general condition. Cyanosis disappeared, breathing became quieter, the pulse slowed and became stronger and delirium and stupor cleared up rapidly. These changes usually occurred within four to twelve hours following the treatment. Whenever the convalescent serum was given early enough and in sufficient dose (50 c.c. to 100 c.c.) the effect on the temperature curve was marked. A slight rise of  $0.2^{\circ}$  to  $0.5^{\circ}$  occurred within a half- to one hour, followed in from one to four hours by a marked fall of from two to three degrees. Any subsequent rise to the original height was always caused by some complication. Usually the fever fell to normal by a swift lysis. Small doses of 25 c.c. may often be sufficient, but larger doses are more surely active in the long run. The intravenous method was almost exclusively used. Four cases were treated with normal serum or a mixture of normal and convalescent serum. While the general improvement occurred, it was much slower and less marked and in 1 case the temperature alone was affected and the general condition remained the same. The authors report the recovery of the most severe case they have ever seen, by repeated injections of the convalescent serum. The child recovered with evidence of degenerative changes in the central nervous system, probably due to the severity of the infection which the serum was not quite sufficient to counteract. A *résumé* of their technic follows the article.

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**Influenza Meningitis.** —ALAN BROWN (*Canadian Med. Assoc. Jour.*, 1915, v, 1076) reports 2 cases of influenza meningitis in children, emphasizing that the influenza bacillus is a not infrequent cause of meningitis. The most prominent and invariable characteristic of this bacillus is its hemophilic property, and next to this its pleomorphism. It may be considered as conclusive that a pseudo-influenza bacillus does not exist. This bacillus is capable of causing inflammation of the serous membranes anywhere in the body. The upper respiratory tract appears to be the most frequent portal of entry into the body. In the cases reported the meningitis developed during an attack of clinical influenza. In 1 case blood culture during life showed a pure growth of influenza, as did also cultures from the brain, heart's blood, left lung and mastoid taken postmortem. The only effect of influenzal serum injected intraspinally was an increase in plagiocytosis. In this case the path of infection was apparently through the ethmoidal plate with practically no involvement of the lungs. The character of the spinal fluid in this condition is fairly uniform, being cloudy, depositing a whitish-yellow sediment and becoming more purulent as the disease progresses. Polymorphonuclears are increased. The morphology of the bacilli vary greatly. Lumbar puncture gives early and correct differential diagnosis in this disease. It is doubtful whether the bacilli are ever present in a clear spinal fluid. There have been slightly over 50 cases of pure influenzal meningitis reported since 1899. Six are reported to have recovered, 1 following the use of influenzal serum.

**Prophylaxis in Pediatrics; Institutional.**—CARROLL (*Pediatrics*, 1915, xxvii, 439) criticises the plan still in use in many hospitals of keeping in one general ward all classes of cases, surgical, skin, neurologic, orthopedic, etc., mingled with general medical and feeding cases and convalescents roaming almost at will and playing with the much-handled and not innocuous ward toys. The two points in common in all these cases are that all are of a pediatric nature as far as age is concerned, and that their physical resistance to disease has been lessened. The problem presented by this condition of affairs is: Lessened physical resistance plus bacteria, plus a means of transmission, plus proximity equals what? The chance of cross-infection is good. The mortality tables of the ward register tell a very pointed tale. Many patients with fair prospects lose all they have gained at the onset of an unsuspected cross-infection and only two frequently succumb either to the primary or secondary infection. The specific causes of this cross-infection include the diseases of mumps, measles, pertussis and scarlet fever, which have no proven specific factor but which comprise three-fourths of the usual sources of infection in institutional wards. The surgical cases contribute the streptococci and staphylococci, the orthopedic, the tubercle bacillus, the specialties, gonococci and streptococci and the medical types a galaxy of all kinds. The means of transmission comprise the ward furnishings, the hands of the professional attendants, and the toys. Under such conditions even with the best of intentions what can be done in the way of prophylaxis? A greater degree of prophylaxis is secured by the ideal system of a ward composed of units each containing between five and eight patients. Each unit is independent, patients can be grouped under any chosen system, and when infection occurs units can be isolated and the entire health of the ward has not been exposed. When the general ward cannot be dispensed with, medical cleanliness by sterilization of every article used on different patients and of the hands of the attendants will reduce the chance of infection proportionately to the degree to which it can be observed.

## OBSTETRICS

UNDER THE CHARGE OF

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**The Treatment of Abortion Complicated by Fever.**—BENTHIN (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 2,) refers to his previous publications and the value of expectant treatment in cases of abortion complicated by fever. He then reported a morbidity of 29 per cent. and a mortality of 9.8 per cent. by active interference, and a morbidity of 9.8 per cent. and a mortality of 0.9 per cent. by conservative treatment. In the presence of the dangers from hemolytic

streptococci, interference is especially dangerous, for in the cases treated by active interference the mortality was 31.2 per cent., whereas by conservative treatment the mortality was nothing. In 23 cases where hemolytic streptococci were present in the uterine cavity, 20 had fever after some interference with the uterus. He quotes 5 cases treated by curetting, of whom 1 died and in each instance, the temperature rose markedly after the exploration of the uterus. His experience shows a mortality in those cases having hemolytic streptococci, treated by active interference, of 18 per cent. In a series of 19 irrespective of the variety of germs present, treated by exploration and evacuation of the uterus by curette and finger, the mortality was 73 per cent. The writer collects a considerable number of statistics which need not be quoted, but which show distinctly that in abortion complicated by fever, interference with the interior of the uterus should be avoided. He described 3 cases in which the uterus was cleared out because it was suspected that placental pieces remained and in which death followed. Autopsy showed in each instance peritonitis and pyemia. If one could be sure that the streptococci present in the uterus in a case of abortion complicated by fever were not hemolytic, and there arose some occasion for interference, one need not hesitate under these circumstances to do so, with the probability of a good result, but in the presence of hemolytic streptococci, interference should not be practiced. The finger only should be employed and the curette should not be used. While there are many theoretical considerations which would urge the universal emptying of the uterus in abortion complicated by fever, the clinical results of the expectant treatment are so markedly extraordinary that certainly a thorough trial of this method is indicated.

**Auto-infection.**—BENTHIN from Winter's Clinic in Königsberg (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 2) discusses this question in the light of his practical experience. There are many factors alleged to militate in favor of auto-infection and they are not, as a rule, sharply defined. One of the first statements commonly made concerning this subject is that auto-infection occurs in those cases where infective bacteria were not artificially placed within the body. This, however, does not explain all cases, as it is not possible to give the origin of infective germs found in the vagina, and yet their presence during pregnancy is undoubted. While it is often asserted that bacteria introduced within the vagina in pregnancy soon disappear, on the other hand, Benthin has used vaginal injections of 5 per cent. lactic acid for weeks and has found hemolytic streptococci at the end of the time. As regards the diagnosis of such a condition, Winter relies primarily upon bacteriological examination. A clearly drawn distinction must be made between endogenous and exogenous infection, and one must recognize also clearly the presence or absence of pathogenic bacteria. Cases where there is no doubt that pathogenic bacteria were present in the region of or near the infected area before the beginning of the disease must be considered as auto-infection. Where one cannot prove in this way that bacteria were present before the outbreak of infection, the cases must be classified as those infected without. It is not sufficient to isolate bacteria, but control cultures are required. This doctrine raises the question, naturally, of the meaning of Aschoff's theory of auto-infection. The presence of pathogenic bacteria in the

secretions of healthy persons, the varying import in prognosis with such persons, the frequency of infection with bacteria produced in the body itself, are all questions which stand or fall with the doctrine of auto-infection. Clinically, bacteriological examination has shown that pathogenic bacteria which develop late in the puerperal period as the cause of septic infection were frequently present before labor. The sort of bacteria is of importance, as the hemolytic streptococci are obviously the most virulent. The prognosis in a given case may often depend upon the presence or absence of repeated examinations and trauma sustained during operation. The reports of the Frankfort Clinic, showing that the presence of the hemolytic streptococci had no especial influence on puerperal morbidity and mortality are not borne out by others. In a series of obstetric operation upon patients in whom hemolytic streptococci were present before the operation, 33 per cent. developed puerperal infection, while in cases in which the hemolytic streptococci were not present, but 14 per cent. developed puerperal sepsis. It is obvious that in those cases where there is reason to suspect the presence of streptococci before labor, that the best results will be obtained as in the Frankfort Clinic, when examinations are made by the rectum only and when vaginal examinations and explorations are conducted as rarely as possible. We must, however, recognize the series of cases of auto-infection in which bacteria make their way upward from the vagina into the tissues of the uterus. In gynecological cases the spontaneous ascent of bacteria is comparatively rare and unimportant. Endometritis may be present but whether lesions in the parametra result in this manner cannot well be known. Where, however, operations are undertaken, auto-infection is a frequent cause of septic disease. Where before operation hemolytic streptococci are present in great number, the prognosis is especially bad. It is interesting to observe that infective bacteria may be present in pregnant women in the mucous membrane of other than the generative organs. Thus we frequently find them in patients who have recovered from some definite infection and usually saprophytic germs are those present. The nasal mucous membrane is a frequent home for infective bacteria. Thus in 111 cases examined, Haslauer found but 8 free from bacteria. The staphylococci are most often there; also the pneumococcus. Streptococci are sometimes found and in Haslauer's 111 cases, in nasal cavities supposed to be normal, streptococci were present in 32; diplococci in 37; staphylococci in 47, diphtheria bacilli in 24. In 57 cases in which the nasal mucous membrane was apparently normal, Besser found streptococci seven times and yet recovery after operations upon the nose is usually undisturbed by septic infection. Where however, streptococci are present, such may not be the case. Thus 7 out of 10 of these cases had fever and infection after operation. After the removal of adenoids, fever has been reported in from 38 to 50 per cent. of cases and general septic infection and not infrequently infection of the sinuses. In the mouth and about the jaws, the *Streptococcus pyogenes* and diphtheria bacilli have been found. In 200 cases streptococci were abundant. While in the normal nose hemolytic streptococci were not found, in the mouth and jaws they were present in 30 per cent. of cases. Others detected the *Streptococcus pyogenes* in from 5 to 62 per cent. of cases. Where the vessels are hypertrophied

there is usually a pure culture to be obtained. In angina hemolytic streptococci have been frequently observed. The ear records of otological societies and their papers upon the subject show that the actual chamber of the ear should be sterile, but, when once infected or inflamed, bacteria are always present, of which streptococci are the most significant. In 292 cases of otitis media Liebmann found streptococci in 189, and in 19 pneumococci. Other observers report bacteria in other portions of the ear quite frequently. In 1907 Süpfle found *Streptococci pyogenes* in 60 per cent. of cases of otitis media. In chronic middle-ear disease bacteria are also present. In the eye, one must remember that the conjunctival sac is well adapted to harbor infective germs. Kraupa found but 33 per cent. sterile in a considerable number. Again the streptococcus is the important germ, ranging from 23 to 43 per cent. Where streptococci only are present, their presence does not seem to militate against the success of operations, but streptococci forbid operation so long as they are present. Kraupa believes that by using oxycyanate of mercury 1 to 5000 he can secure a sterile condition of the conjunctival sac in a few days. That this preliminary treatment is valuable is shown by Elshnig and Ulbricht, who in 179 cataract operations had but 0.6 per cent. of failure through infection, while in 137 cases where no prophylactic measures were taken, and various operations were done, the morbidity was 5 per cent. The practical conclusion remains that, under some circumstances, bacteria which are present in the secretion of a mucous membrane may cause disease after some interference with this membrane, whether by surgical procedure or by parturition. It is important to recognize, if possible, the sort of bacterium which is present. The fact that fever may not be present does not positively prove the absence of danger, for some most severe infections are afebrile. It is important to know that when fever develops it is probably caused by germs which were in the vagina before labor. The reason for ascertaining the precise sort of bacterium lies naturally in the effort to produce sera or vaccines which may be of service to the patient. Benthin has no especial confidence in vaginal injections given before or during labor and believes that we cannot mechanically remove every bacterium found in the vagina. Unquestionably, septic disease would become more and more infrequent as external asepsis is carried out thoroughly, and unnecessary examinations and manipulations are avoided. It will be a very difficult thing to entirely overcome auto-infection, but the effort should certainly be made. No consideration of the subject of auto-infection in parturient women can be complete without reference to decaying teeth. The notable tendency of dental caries to increase rapidly during pregnancy naturally suggests this fact. In the reviewer's experience a primipara passed through a spontaneous normal labor under antiseptic precautions and without much injury. On the fourth and fifth days, with normal lochia and secretion of milk, her temperature rose to 102° and 103° and 104°F. No pelvic condition accounting for this could be found, and a thorough search was made of the patient's body for some focus of previous infection. The patient had been to her dentist very shortly before confinement and was pronounced in good condition. While pressing along the jaw a tender point was found, and the patient stated that some years before she had there had inflammation about

the root of a tooth. Her dentist was summoned, who incised at this point, obtaining about 2 drams of exceedingly foul pus. The emptying of this pocket was followed by the disappearance of the fever. Ultimately, so extensive was the caries, that a piece of the jaw-bone had to be excised by a surgeon to secure a sound healing.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Treatment of Uterine Perforation—Radical or Conservative.**—It is easy to lay down the dictum that perforation of the uterine wall during an attempt to evacuate retained secundines should never occur, but so long as the operation is performed, especially by those not especially trained in gynecological surgery, and often under unfavorable surroundings, there are bound to be occasional cases of perforation of the softened uterine wall by the curette or placental forceps. It is commonly believed that such injuries are rarely fatal unless accompanied by distinct evidence of injury to some abdominal viscus, and may therefore be treated by a "watchful waiting" policy; while this is undoubtedly true in certain cases, the fact has been forcibly brought out in a recent article by SCHWEITZER (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, xlii, 148) that in the majority of cases, the condition is more serious than is often believed. Schweitzer has collected from the German literature of the last five years 105 cases, reported by 49 different surgeons: notwithstanding the fact that most of these cases were brought under the care of trained gynecologists, the total mortality of the entire series was something over 25 per cent. In no less than 48 of the cases had injuries to the intestines occurred, with 18 deaths; there were 6 cases of simple intestinal prolapse, with 1 death; 10 of omental injury, with no deaths. In 2 cases the tube and ovary were injured, in 1 the bladder injured (died), and in 1 the ureter was torn loose both at the renal and vesical end (recovery after nephrectomy). In 1 case even the cartilage at the sacral promontory was torn loose. The dangers that may beset the expectant method of treatment for cases of uterine perforation are shown by the fact that of 17 cases so treated, 9 died, a mortality of over 50 per cent., much higher than that of the series as a whole, or of the cases treated by laparotomy. Of these 9 fatal cases, 6 died from peritonitis, 1 from general sepsis, 1 in collapse, 1 from cachexia following a utero-intestinal fistula. Of those that recovered, only 2 patients came through without serious complications; in three instances there were utero-intestinal fistulae which healed, in 1 intestinal adhesions caused obstruction, for which subsequently a laparotomy had to be performed; in another, a pelvic abscess formed which required drainage,

etc. From these figures, the author draws the conclusion that the only cases which may safely be treated expectantly are those in which the perforation is evidently small, the uterus completely empty and apparently not infected, and in which no evidence of intestinal injury is present. All others, he thinks, should be subjected to immediate laparotomy. With regard to the treatment of the perforated uterus, once the abdomen is opened, Schweitzer thinks the best policy is in most cases to remove it, rather than to try to repair the injury by suture, since the latter procedure cannot prevent a secondary infection of the peritoneal cavity if the uterus is infected, a condition that it is impossible to exclude in cases of this sort. The statistics that he has been able to collect on this point, while based on rather small series of cases, bear out this contention as far they go. Of 12 cases treated by suture, 1 died (8 per cent.); of 24 cases treated by hysterectomy, 1 died (4 per cent.). With regard to the prevention of injuries of the class under discussion, the author insists that the curette should never be used in cleaning out an abortion, and placental forceps only to remove pieces of material that have been completely freed from the uterine wall by the finger. He insists that all the actual work shall be done by the finger only, and very rightly condemns utterly the practice of indiscriminately curetting or using the forceps without ever introducing the finger through the cervix to palpate the interior of the uterus. If these simple principles were more generally observed, he says, we should have practically no cases of perforation to treat.

**Treatment of Pelvic Inflammation with Ultraviolet Rays.**—The success obtained by the treatment of surgical tuberculosis with ultraviolet rays suggested to FROMME (*Zentralbl. f. Gynäk.*, 1915, xxxix, 598) to try the same method in chronic gynecologic inflammations. The rays are obtained from a so-called "artificial sun lamp," which is apparently of the mercury vapor type. The rays are applied directly to the abdomen, the remainder of the body being covered to prevent injury. The first application lasts, as a rule, only one and a half minutes with the lamp 75 cm. from the skin; after a couple of days a second exposure of two to two and a half minutes is given with the lamp only 60 cm. from the skin. Then on following days the exposures are increased by two or three minutes each day until an exposure of twenty minutes has been reached, the lamp being at the same time gradually brought to within 40 cm. of the skin. A marked hyperemia always occurs after the first treatment, which gradually gives places to to a brown pigmentation, practically a sun-burn. This, however, disappears after cessation of treatment. Fromme reports that he has treated by this method 25 cases of pelvic inflammation, in nearly all of which were pus tubes the size of the fist. About half of these patients are still under treatment; 9 have been discharged as cured after an average of about 15 exposures; in 2 instances no benefit was obtained. In the ones considered cured all traces of the adnexal enlargements had disappeared. All these were treated as out-patients, merely coming to the hospital for the actual treatment, their ordinary life being in no other way interfered with. In addition to the inflammatory cases, 6 of pruritis vulvæ were subjected to the treatment, with 2 definite cures, and marked improvement in the other 4, all of whom are still



under treatment. Fromme thinks, as a result of these experiences, that the ultraviolet rays may be found to have a considerable field of usefulness in gynecology.

**Ovarian Transplantation.**—This operation, which has been discussed a number of times in these pages in the past few years, forms the subject of a recent clinical report by CHALFANT (*Surg., Gynec. and Obst.*, 1915, xxi, 579), which is based upon 32 cases drawn from his own experience and that of Dr. Simpson, of Pittsburg. In all these cases the transplantation was autoplasmic, *i. e.*, the patient's own ovarian tissue was used for the graft. The purpose of the operation is, of course, to conserve to the woman the internal secretion of the ovaries in those cases where either from infection or damaged blood supply it does not appear safe to leave the ovary in the peritoneal cavity. The technic observed by Simpson and Chalfant was as follows: "After the ovaries were removed, a portion or all of the better one was kept in normal salt solution at body temperature until the operation proper was completed. Then a small incision was made through the skin about two inches inside the anterior superior spinous process of the ilium. A pocket was made in the subcutaneous tissue by spreading a hemostatic forceps, and into this pocket a section from the cortex of the ovary was inserted and the skin closed by plain catgut suture. The same technic was followed in all cases, except that in some a transplantation was made on both sides." This particular location for the graft was chosen because of accessibility, both at the time of operation and subsequently, good blood supply, and absence of danger of intraperitoneal or retroperitoneal involvement, if the graft should be already infected at time of implantation. Of the 32 patients reported upon, 13 had one ovary left in its normal position, and should therefore, it would seem, be dismissed from further consideration. In only two instances were both ovaries removed and the uterus allowed to remain; one of these started menstruating four months after the operation, and continued regularly for six months, since which time there has been no flow, with moderate menopausal symptoms. The other patient never menstruated, and had quite severe menopausal symptoms. Of the 17 patients from whom the uterus and both ovaries were taken, 5 gave evidence of apparent continued function of the graft, as shown by variations in size and increased tenderness. With regard to the presence or absence of menopausal symptoms, which forms, of course, the crux of the situation, only 17 patients are tabulated, and it is not quite clear whether any of these may belong to the first group, in which one ovary was left *in situ*. Of the 17, however, 10 per cent. had no menopausal symptoms, 41 per cent. slight, 29 per cent. moderate, and 18 per cent. severe. In order to have a basis of comparison, the authors sent out a series of letters to patients from whom both tubes and ovaries had been removed, but in whom no transplantation had been done. Tabulation of 40 replies showed that 10 per cent. of these likewise had had no menopausal symptoms, 17 per cent. slight, 20 per cent. moderate, and 52 per cent. severe. While admitting that the above series of cases are too small from which to draw any definite conclusions, the authors consider that the comparison indicates that transplantation does lessen to some extent the severity of the artificial menopause.

## OTOLOGY

UNDER THE CHARGE OF

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**Mastoiditis and Erysipelas.**—The fact that the mastoid operation may be performed with expectation of good results in the face of an erysipelatous inflammation has been demonstrated in primary healing under this condition but the possibility of a favorable outcome under apparently subversive conditions is emphasized in two cases reported by MAHER (*Bull. d'oto-rhino-laryng.*, xvii, 6), who had made a series of observations of operative cases under coincident erysipelatous manifestation and had been surprised at the inversive effect of the apparent complication. In the first instance a woman, thirty years of age, had an acute inflammation of the right middle ear, accompanying a nasopharyngeal infection and a right maxillary sinusitis. The patient was, moreover, suffering from a puerperal infection; paracentesis of the drum-head failed to lower the temperature or to lessen the mastoid pain and tenderness, and an antrotomy was done with complete resection of the mastoid apophysis. Two days later an erysipelatous macule appeared followed by a chill and rise in temperature and this was followed by a bilateral cervical adenitis which broke down and a pleural suppuration requiring thoracentesis. To this was added a marked albuminuria, constituting a serious clinical picture. The erysipelas completed its cycle of the face, the neck, and part of the trunk, the accompanying suppuration from the mastoid being abundant, daily dressings with sterile water were continued throughout the disease; the patient was extremely weak but, with the subsidence of the erysipelas this condition ameliorated, the postaural wound rapidly closed, and in fifteen days cicatrization was complete and the patient was fairly convalescent in all respects. The second case was that of a woman, thirty-eight years of age, with an ozena, who had complained of pain in the ear and, in a sudden attack of vertigo, had fallen forward. Examination showed the mastoid to be tender over the antrum and at the apex and that there was a marked bulging of the posterior superior canal wall almost to the extent of touching the opposite wall. Under antrotomy and removal of the major portion of the outer mastoid cortex, the cavity and the antrum and aditus were found to be filled with fetid fluid and granulomata, the lateral sinus was intact as also a considerable area of exposed dura. After operation and on the morning of the following day, the temperature remained stable but, on the afternoon of that day, it suddenly rose, increasing still further on the following day coincidently with the manifestation of a severe chill and the appearance of an erysipelatous blush upon the face, which rapidly spread to the scalp and neck; the temperature continued high for three days, the patient became excitable and delirious, requiring a straight jacket, and developed an acute mania lasting nearly a

week and accompanied by marked albuminuria. During the course of the erysipelas, the dressings of sterile water and alcohol were continued daily but the wound remained fungous and areas of exposed bone suggested the possibility of later sequestræ. As the erysipelas disappeared the general condition improved and the wound became clean, healing rapidly within a few days without elimination of the expected sequestræ. In still another case of mastoid operation in a child with slow closure of the postaural wound, the appearance of an erysipelas seemed to have a stimulating effect and the wound became cicatrized in a few days.

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**Massage of the Tympanopharyngeal Tube.**—Tubal massage, as an adjunct to the treatment of swelling of the tubal mucosa and of incident middle-ear disease has been commended by various writers advising deep manipulation of the cervical muscle, beneath the auricle, without, or in combination with, correlative movements of the buccal and pharyngeal muscles; more direct massage has also been applied directly to the lateral pharyngeal walls by means of sounds or by the introduction of the finger covered with a rubber cot. The massage through the external muscles is comparatively ineffective because of the resistance offered and because of the impact of the pressure along the long axis of the tube and a minimum of influence exorable upon the tubal mucosa; the more direct massage through the mouth possesses decided advantages, but is open to the objection, in a large number of cases, of a maximum of discomfort from the necessary manipulation of the soft palate and the lower, and reflexly sensitive, lateral pharyngeal walls. P. J. MINK (*Ztschr. f. Ohrenh.*, 1915, lxxii, 3) therefore utilizes for massage purposes the pharyngeal applicator devised by him in 1906, consisting of a silver or white-metal rod 20 cm. in length and 1 mm. in diameter, contoured like a nasal catheter, slightly curved, to rock over the nasal septum, and bent sharply upon itself at the outer end in such a manner as to make it a tactile as well as a visual index of the direction of the tip of the sound which, wound with cotton and dipped in glycerine, is introduced, after the fashion of a nasal catheter, carried as far back as the posterior pharyngeal wall, then turned outward into the post-tubal fossa, and forward over the tubercle into the mouth of the tube, the whole tubal region being by this means easily manipulable.

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**Mastisol.**—THEIMER (*Ztschr. f. Ohrenh.*, 1915, lxxii) commends the use of a mastic solution in the preparation for surgical operations upon the ear upon the ground of personal experience in its use as an adjunct to other measures for sterilization of the operative field. That the customary methods of sterilization, following shaving of the side of the head, consisting in washing with soap and water by means of a stiff brush, with ether and with benzine are ineffectual has, in the opinion of the author, been sufficiently proved, while the disinfection of the skin by painting with tincture of iodine is open to certain objections, although the attained asepsis is complete, but in many cases the application is not well borne by the skin, which becomes irritated and eczematous and the sutured or clamped edges of the incision swollen and less well apposed. The value of the solution of mastic in benzol lies mainly in

the fact of its rapid fixation and virtual arrest of the bacteria in the skin, the procedure, in preparation for a mastoid operation for instance, consisting in the scrubbing of the previously shaven operative field with soap and water, then with benzine or ether, and finally the painting of the surface and of the adjacent hair with the mastic solution, the result being not only a firm fixation of the hair and security against its invasion of the operative field but so effectual a sterilization of the skin as to greatly favor primary healing in the cases in which it was employed.

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**Good Hearing after Total Destruction of the Mastoid Process by Means of a Projectile. Total Deafness, Traumatic Rupture of the Drum-head and Complete Facial Paralysis Following Concussion of the Mastoid Process.**—Two contrasting cases of the effect of gunshot wounds are reported by BECK (*Monatsschr. f. Ohrenh.*, 1915, xlix) as illustrative of a class of injuries now being received for investigation and treatment at base hospitals. The first patient, aged twenty-four years, had been struck by a bullet on the left mastoid process with nearly complete disruption of that bone and with passage of the projectile apparently inward and forward. On the left side of the nose there was a scar which suggested the point of exit, but there was no supporting evidence found under the Roentgen-rays and the superior maxillary on the corresponding side was free. Immediately after the injury the patient was not unconscious; he made his way unaided to the nearest dressing place and four days later was presented for examination in Vienna, very weak, with moderate degree of fever and with very purulent discharge from the external ear and from the wound in the mastoid process. Water syringed into the middle ear flowed free from the mastoid wound. Within the mastoid opening numberless small sequestræ could be easily felt and removed by means of the forceps, and after thorough cleansing of the auditory canal a fracture was determinable on the posterosuperior bony canal wall, from which place numerous granules so occluded the canal as to prevent a view of the drum-head; there was no spontaneous nystagmus. The right ear heard normally, the left ear heard a light whispered voice at a distance of seven meters and, on that side, there was complete facial paralysis in all three distributions. On the day after examination the patient had a rise of temperature with general malaise; the wound was carefully re-examined and still more mechanical sequestræ removed. The extent of the local injury and the character of the general symptoms suggested the possibility of a sinus thrombosis, but the condition of the skin in the neighborhood of the wound indicated the beginning of erysipelas. Operative interference was deferred with the result that on the next day the erysipelas had become definitely pronounced. The later operation resulted in the removing of the sequestræ, thorough cleansing and subsequent healing, but the facial paralysis remained unchanged, and the hearing was unimproved. In the second case, of a soldier, aged twenty-two years, the projectile has entered the mouth through the right cheek and made its exit through the ear behind and under the tip of the mastoid process. The patient was unconscious for twenty-four hours after the injury. On examination there was found, in the right drum-head, in the posteroinferior quadrant, a triangular perfora-

tion with a moderate amount of discharge only. The left ear was normal of condition and of normal hearing; the right ear was completely deaf and there was complete facial paralysis. The vestibular reaction was present as in the preceding case. This case remained five weeks under observation, during which time there was no change in the hearing and the Roentgen-ray examination of the mastoid process showed no fracture or splitting of the mastoid tip. In view of the complete paralysis of the patient and in view of the direction of the course of the projectile it is supposable that the bullet grazed the tip of the mastoid process and so severed the facial at its point of exit from the bone; the complete loss of hearing being the result of the incident shock. The contrast between this and the preceding case is that of a normal mastoid process with complete loss of hearing and of destruction of the mastoid process with a fairly good remnant of hearing.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**The Influence of the Exposure of the Roentgen-rays upon the Formation of Antibodies.**—The destructive action of the Roentgen-rays upon the lymphatic tissues has been demonstrated by many. In part the effect of this can be shown in the diminution of the leukocytes in the blood. It has been noted that mice and guinea-pigs when exposed to the Roentgen-rays showed a variation in the susceptibility to particular infections. Some have found that the direct application of the Roentgen-ray to infected foci assisted the destruction of the bacteria. On the other hand, others were more susceptible to various infections. SIMONDS and JONES (*Jour. Med. Res.*, 1915, xxxiii, 183) carried out a series of experiments upon rabbits. These were exposed to Roentgen-rays for ten to fifteen minutes daily for a period of three weeks. They were then inoculated with *B. typhosus*. It appeared that the animals were less resistant to the immediate effects of the infection than the controls. In studying the antibodies quantitatively, the authors found that the production of agglutinins was appreciably less, while the quantities of bacteriolysins and opsonins were not altered to any marked degree.

**Further Investigations into the Etiology of the Protozoan Disease of Turkeys, known as Black Head.**—The present investigation was a continuation of the work carried on by the author in 1895. Relatively few studies have been made upon this important disease. THEOBALD SMITH (*Jour. Med. Res.*, 1915, xxxiii, 243) had previously pointed out that the pathology of the disease was not especially characteristic. The lesions are almost limited to the ceca and the liver. Occasionally too, the liver lesions may be absent. At times, however, pathological lesions are more disseminated in the intestine. The most striking feature is the filling up of the lumen with a tough leathery mould made up of concentric layers. This material may be firmly attached to the mucosa. The disease attacks both old and young, being most fatal in the first two months. The author demonstrated protozoan parasites which, to some extent, resemble and are confused with coccidia. These parasites appear in the mucosa and submucosa in which a chronic inflammation leads to much thickening. The parasites appear in large numbers lying between the cells of the various layers. The material within the bowel consists of inflammatory exudate. Similar protozoan diseases have been reported in wild and domestic birds. Animal experiments in the transmission of the disease have not been uniformly successful. Infected materials fed to healthy animals do not necessarily lead to infection. The rapid course of the disease and the lesions appear to be due as much to the mechanical disturbances accompanying the invasion and distribution of the organism as to the toxic action of the parasites. The invasion of the liver is through the blood, the parasites being transported either freely or in phagocytes. It is not known whether the parasite requires an intermediate host.

**The Sterility of Bile under Normal Conditions.**—TODA (*Arch. f. klin. Chir.*, 1914, ciii, 407) studied the character of the bile to determine the presence of organisms under normal conditions. He obtained samples of bile from 35 humans and 8 dogs. These were all sterile. He then undertook an investigation to determine the bactericidal properties of the bile. He found that *B. coli* could grow in fresh human bile, but were somewhat inhibited by bile from dogs. Likewise bile forms a good medium for the growth of *B. typhi*, which remained living ten weeks in this material. *B. paratyphosus A* reacts in a manner similar to *B. typhi*, while *B. paratyphosus B* and the dysentery bacillus are inhibited by the presence of bile. The *B. cholera* flourishes well in human bile, while *B. pyocyaneus* is rapidly destroyed. The staphylococci and streptococci are not greatly influenced by the bile in the medium, but pneumococci are rapidly killed off. Another interesting finding was that fresh bile appeared to enhance the virulence of *B. coli*.

**Contribution to the Study of Endemic Goitre.**—Much has been written about the endemic character of goitre. MESSERLI (*Centralbl. f. Bakt. riol.*, 1911, lxxv, 3) gave water from different sources to white rats. Some were given water from the supply at Lausanne where endemic goitre is unknown, others were given water from Payerne, where goitre is very common. The latter is a surface water with a high bacterial content. The animals which were given the Lausanne water showed no changes in the thyroid, while those rats receiving water from

Payerne showed both macroscopic and microscopic evidence of thyroid hyperplasia. In various instances the enlarged thyroid could be recognized as true goitre. The author believes that his results indicate further evidence that endemic goitre is the result of improper drinking-water with definite bacterial pollution

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**Basedow's Disease and the Thymus.**—KOCHER (*Laugenbeck's Arch.*, 1914, cv, 924) in a surgical material of 979 cases has never seen a case of Basedow's disease in which hyperplasia of the thyroid was absent. Nevertheless, a considerable number of Basedow's cases show a pathological change in the thymus. Thymus hyperplasia in Basedow's disease is more common in the young than in the old, the thymus varying in weight from 15 to 50 grams. The hyperplasia of the thymus in Basedow's is histologically similar to the not uncommon thymus hyperplasia observed in children. It is interesting that thymus hyperplasia is at times more frequent in particular families and localities than in others. It would appear that in some cases, the thymus hyperplasia is more or less coincident with a subsequent thyroid disease, and hence has no direct relation to the occurrence of Basedow's. The author suggests that the thymus hyperplasia may bear some relation to the hyperplasia of the adrenal. He believes that with the onset of Basedow's there is not uncommonly a cellular hypertrophy in the medulla of the adrenal as well as occasionally in the thymus. Some of the symptoms of Basedow's may be referable to such changes occurring in other organs. He is insistent, however, that a typical Basedow's without thyroid change and referable only to the thymus hyperplasia does not occur.

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**A Bacterial Study of an Epidemic of Septic Sore Throat.**—An interesting epidemic of septic sore throat, traced to the milk supply of the community, is described by KRUNWEIDE and VALENTINE (*Jour. Med. Res.*, 1915, xxxiii, 231). The epidemic occurred during June, 1914, in Rockville Centre, S. I., a village of 4,250 inhabitants. The suspected milk came from a dairy (Oceanside) and supplied about 1200 quarts a day. Of the 232 cases of septic sore throat, 205 cases obtained their milk from the Oceanside dairy. In other words, the milk supply making up 25 per cent. of the total contained about 90 per cent. of the cases. On investigation, it was found that at the Oceanside dairy the daughter of the owner developed a sore throat April 16, 1914. On May 9, the owner became infected and subsequently the driver. Both the owner and the driver took care of the milking. The epidemic broke out about June 1, 1914, and lasted until about June 14. Bacteriological investigation was then undertaken including moist swabs from the throats of persons at the dairy, a culture from a complicating case of peritonitis of one of the cases, and samples of milk from each cow in the dairy. The milk obtained from five of the cows showed a moderate number of streptococci. One cow showed a mastitis, while another animal gave an enormous number of streptococci in the milk. On examining the cultures made from the cow showing the excess number of bacteria, a hemolyzing streptococcus was obtained similar in cultural characters to that obtained from the throat swabs and from that of the case of peritonitis. Cultures from the other cows

showed only non-hemolyzing types of streptococci. The facts of the case would, therefore, suggest that the infection was milk-borne, but of human origin. The cow became infected with a human type of streptococcus, although it showed no evidence of a mastitis. From these results the authors believe that in tracing such an epidemic, efforts should be made to find cases of sore throat in those engaged in milking, rather than cases of mastitis in the cows.

**The Relation of the Adrenals to Cholesterin Metabolism.**—A number of English authors (Ellis, Frazer, Gardner) have demonstrated that the cholesterin content of the body is in direct relation to the cholesterin intake of the food. It was shown by them that there was no cholesterin synthesis by the body tissues. On the other hand, it was demonstrated by others that a hypercholesterinemia is not uncommonly observed in pregnancy, diabetes and nephritis in which there is also a definite increase in the cholesterin content of the adrenals. This finding was interpreted by some to indicate a definite production of certain organs, particularly the adrenal of cholesterin compounds. Some experimental work was even offered to show that the adrenal had much to do with the amount of cholesterin in the blood stream. ROTHSCHILD (*Ziegler's Beiträge*, 1915, ix, 39) studied the subject experimentally, using rabbits. Because of the similar functional property of the corpus luteum cells with those of the adrenal, male animals only were used. Careful estimations were made in control animals to determine the normal quantities of cholesterin in the blood, adrenals and the bile. He then undertook the extirpation of one or both adrenals noting in each instance the variation in cholesterin content of the blood, the remaining adrenal and the bile. Upon removal of one adrenal the cholesterin content of the blood rises rapidly within twenty-four hours, while the content of the remaining adrenal is depressed during the first few days, subsequently again assuming the normal level. On removal of both adrenals, the cholesterin content of the blood rapidly increases. This would indicate that the blood cholesterin may increase without the participation of the adrenals and that the hypertrophy of the adrenal with increased cholesterin content is a secondary process. The rapid increase of cholesterin in the blood is accounted for in rapid tissue destruction or its liberation from fat depots. The cholesterin balance of the blood is maintained by the excretion of cholesterin in the bile. The author cannot find any support for the contention that the adrenals manufacture cholesterin for the body. It appears more probable that the adrenal is merely an intermediate organ which has to do with the disposal of a certain quantity of the cholesterin of the blood. His final conclusion, that Addison's disease is related to a destruction of the adrenal cortex and not its medulla, is not clear in the evidence presented.

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ORIGINAL ARTICLES

**THE CAUSES OF DEATH IN DIABETES.<sup>1</sup>**

BY ELLIOTT P. JOSLIN, M.D.,

BOSTON.

(From the Nutrition Laboratory of the Carnegie Institution of Washington in Boston,  
and the Department of Medicine of the Harvard Medical School.)

WITH the lapse of years the conviction has grown upon me that the life of a diabetic patient might be prolonged and that coma was an avoidable accident, and yet I know of no cure for diabetes and I claim no patient cured. The results of the investigations conducted with Professor Benedict at the Carnegie Laboratory upon the utilization of carbohydrate in diabetes, and reported here last spring,<sup>2</sup> greatly strengthened that belief, for they proved that even the severest diabetic retained some power to burn carbohydrate. Then, too, in these last few months I have been unable to find any uncomplicated case of diabetes of long or short duration which has failed ultimately to show at least a small positive carbohydrate tolerance. The simultaneous observations of the Russell Sage Laboratory at Bellevue Hospital and the Carnegie Nutrition Laboratory showing that the respiratory quotients of severe diabetic patients rise following a prolonged fast, although not fully explained, are encouraging. And, finally, I must acknowledge that the fact that under simple prolonged fasting treatment no death from diabetes occurred among my patients at the New England Deaconess' Hospital for 350 days, has deepened the impression above expressed.

<sup>1</sup> Delivered at New York Academy of Medicine, December 21, 1915.

<sup>2</sup> Harvey Lecture, Delivered March 13, 1915. Also published in *Arch. Int. Med.*, 1915, xvi, 693.

Enthusiasm governs the present, but facts the past. Consequently, I have endeavored to secure the end-results of all the diabetic patients I have seen in private practice from the first case of my student days in 1894 to November 18, 1915. Of these 945 cases, 921, or 97.5 per cent., have been traced, and out of this number 425 have died. The actual causes of death are known to me in all but 5 cases. It is true that many of the patients were seen by me but once, yet this by no means detracts from their interest.

TABLE 1.—CAUSES OF DEATH OF DIABETIC PATIENTS SEEN IN PRIVATE PRACTICE ONE OR MORE TIMES FROM 1894 TO DECEMBER 18, 1915.

		Deaths in Number, hospital.	Deaths outside hospital.
A. DEATHS WITHOUT COMA . . . . .	147	2	145
I. Miscellaneous . . . . .	16	0	16
Pernicious anemia . . . . .	1		
Old age . . . . .	2		
Diabetes . . . . .	8		
Cirrhosis . . . . .	2		
Suicide . . . . .	2		
Drowned . . . . .	1		
II. Cancer . . . . .	17	1	16 also 1 with coma.
Face . . . . .	1		
Esophagus . . . . .	1		
Stomach . . . . .	4		
Rectum . . . . .	1		
Liver . . . . .	6		
Bladder . . . . .	2		
Bones (sarcoma) . . . . .	1		
Seat of growth unknown . . . . .	1		
III. Pulmonary tuberculosis . . . . .	16	1	15 also 5 with coma and 2 with infec- tions.
IV. Cardiorenal and vascular . . . . .	62	0	62
Cardiac . . . . .	28		
Bright's . . . . .	14		
Cerebral hemorrhage . . . . .	11		
Arteriosclerosis . . . . .	6		
V. Infections . . . . .	36	0	36
Tonsillitis . . . . .	11		
Pneumonia . . . . .	15		
Influenza . . . . .	3		
Gall-stones . . . . .	1		
Septic and gangrenous legs . . . . .	9		
Carbuncles . . . . .	1		
Acute appendicitis . . . . .	2		
Erysipelas . . . . .	1		
B. DEATHS WITH COMA . . . . .	273	15	258

A. DEATHS WITHOUT COMA. The causes of death of these patients will be discussed under six headings, into the first of which I will place the miscellaneous and uncommon causes.

1. *Miscellaneous.* In this group fall 1 death of pernicious anemia, 2 of old age (aged seventy-eight and eighty-six), 8 of which I can secure no other details than a death report signed diabetes, 2 of cirrhosis of the liver, 1 was drowned, and 2 committed suicide.

Of the latter, one was mentally unbalanced and the other took her life after becoming pregnant a second time soon after an abortion. Today I should not advise an abortion unless vigorous and prolonged treatment failed to render the urine sugar- and acid-free.

II. *Cancer*. Seventeen of the patients died of cancer. The primary growths were in the face, esophagus, stomach, rectum, liver, bladder, and I include 1 case of probably sarcoma of the pelvic bones. The average age at death of these patients was sixty-five years. Cancer apparently developed after the diabetes in 8 cases, and may have developed before or coincident with the diabetes in 7 others. Incidentally, I would say that 2 cases of cancer which have been operated upon are alive, 1 of the bladder and 1 of the uterus. A patient with cancer of the bladder died suddenly of pulmonary embolism nine days after its removal and another with recurrence in the abdominal scar.

III. *Pulmonary Tuberculosis*. Pulmonary tuberculosis was responsible for the death of 16 cases. The medical profession has altogether too pessimistic a view about this complication. When the treatment of the diabetes is faithfully carried out these patients do quite well. The trouble in the past has been that consumption was usually advanced when diagnosed. In a diabetic, temperature, pulse, and respiration give no clue to the diagnosis, and the loss of weight is attributed to the diabetes. One case of tuberculosis died under my very eyes in the hospital without my suspecting what proved to be extensive lesions. That this mistake is common I am convinced because, with my mistake in mind, a few months later, in one of the very best hospitals, I was able to point out advanced but also unsuspected tuberculosis in a diabetic. The detection of tuberculosis in diabetics is aided by a careful study of the family history and an x-ray examination.

IV. *Cardiorenal and Vascular*. Cardiorenal and vascular changes, uncomplicated by coma, caused the death of 62 cases. Of these 28 died of heart disease, in 4 instances suddenly with angina pectoris, 13 died of chronic nephritis, 14 from a cerebral hemorrhage, 6 of general arteriosclerosis, and 1 of pulmonary edema. The average age at death of these patients was sixty-four years. If the methods we employ in the treatment of these same arteriosclerotic conditions in non-diabetic patients are correct, it is difficult to see how modern treatment with restricted instead of forced feeding can fail to prolong the life of these individuals.

V. *Infections*. The advent of an infection lowers the tolerance of a diabetic for carbohydrate and thus increases the severity of the disease. This is an old and reliable clinical fact. It has lately been emphasized by the Chicago School. Case 813, eight years old, sugar-free for eighteen days, developed tonsillitis, and without change of diet a positive carbohydrate balance of 50 grams dropped to 14 grams, with reappearance of acidosis. Recent experiences

with fasting treatment show that in the presence of an infection a diabetic becomes sugar-free very slowly. An infection is an additional load for the diabetic to carry, and to it he often succumbs. If those cases are excluded in which coma was an element the number of deaths from infections is comparatively small, for there were but 36 cases. Of general infections, pneumonia heads the list with 15 deaths and influenza claims 3. Of local infections, septic and gangrenous legs account for 9, carbuncles for 4, and acute fulminating appendicitis for 2.

Thus far we have accounted for 147 deaths. Of this number it is problematical how many could be saved today. Perhaps one death from suicide could be prevented, a little could be accomplished for the cancer cases, the diseases might be arrested in a few and life prolonged in most of the tuberculous, but how effective modern treatment would be upon cardiorenal and vascular conditions in diabetes time alone will tell. But the majority of my diabetics died from another cause, and now let us face it.

B. DEATHS WITH COMA. Coma was fatal to 273 of my cases (64.24 per cent.), thus causing two-thirds of the deaths. During the last fourteen years there have been treated under my personal supervision in hospitals, 273 cases of diabetes, of which 15 have died of coma, making my total deaths in hospitals for this period 17. For many years my attitude toward coma was to consider it the culmination of the diabetes, and after the death of the comatose patient I could honestly unite with the family, the physician, and the nurse in the feeling that no more could have been done. But for me this comfortable creed has passed, and in its place has come the opinion that coma by no means represents the culmination of the disease, that it is not a justifiable accident, and though not in all, yet in most cases it is avoidable. My conception of coma in diabetes cannot better be expressed than by quoting from the charming essay of Moynihan on "Inaugural Symptoms in Abdominal Emergencies with Especial Reference to Duodenal Ulcer," only I shall change the word "ulcer" and the phrase "in the abdomen" to "diabetes," and the word "perforation" to "coma."

With the wording thus changed the text would read: "It is in dealing with the acute catastrophes occurring in *diabetes* that we shall probably derive the most instant and striking advantage from an attentive study of inaugural symptoms. To take a specific example, the onset of *coma* in *diabetes*. But let me first say that a catastrophe of this kind is almost always capable of being forestalled. Though the onset of *coma* in *diabetes* is acute the *diabetes* itself is chronic. It is a disease that has existed for months or years and it has given, in almost every instance, not only sustained evidence of its existence, but a recent warning that the pathological processes engaged in it were becoming more acute. The warning, however, is commonly ignored, because the significance and import-

ance of it are not understood, and accordingly a disaster is precipitated. There are few catastrophes occurring in diabetes that are veritably acute."

Bearing this point of view in mind, may I analyze for you the deaths from coma which have occurred in my practice?

1. *Ether Anesthesia*. Case No. 729, a severe diabetic, three months after her last visit to me, without my knowledge, was taken to a dentist's office, given ether by her physician, and all her teeth extracted. This was on a Monday. She was taken home, became unconscious Wednesday, and died on Friday. I cannot force myself to believe that her death represented the culmination of diabetes, or was even accidental. Case No. 348, before an operation for removal of a prostate, was free from acid and sugar and tolerated 20 grams of carbohydrate. After light etherization followed by fasting, 33 and 41 grams of sugar appeared in the urine on the second and third day of the fast respectively and the ammonia was 3.3 grams. It is true that he recovered, just as all but 6 of 26 patients under my supervision who have had major operations have also done, but the ether lowered his tolerance and made his diabetes temporarily worse. This does not mean that diabetics should not be operated upon, but it demonstrates that ether anesthesia is a burden which a light case of diabetes may easily bear, which may change a moderate to a severe case, and to a severe case may be fatal.

2. *Impaired Kidneys*. Diabetic patients with vulnerable kidneys are peculiarly susceptible to coma because the power of elimination of acid bodies is impaired. You all will recall cases of Bright's disease in diabetes in which an apparently mild acidosis preceded coma. Years ago, Goodall<sup>3</sup> and I pointed out that acidosis was much more easily tolerated by the young than the old diabetics, and this can well be attributed to the deficient kidneys of the latter. Few could void on the verge of coma the five or more liters of urine which with the old alkaline treatment was necessary for recovery, and is recorded to have taken place in those patients who did recover. Coma by no means is confined to the young: thus the percentage of coma in my fatal cases under fifty-one was 67 per cent. and above that age 33 per cent. I could specify several instances of this type and in this group might well be classed a few of the cases of death in pregnant women.

3. *Infections*. Already attention has been called to the fact that an infectious process renders the diabetes more severe. A considerable percentage of the cases of coma occurred in connection with either general or local infectious processes. It not infrequently happens that the infection is not recognized. Better statistics

<sup>3</sup> The Clinical Value of the Estimation of Ammonia in Diabetes, Boston Med. and Surg. Jour., 1908, clviii, 646.

upon this point and in general about the circumstances attending coma should be accumulated. Thus, Case No. 836, seen in consultation one evening, was found to be in partial coma, but I was able to demonstrate to the physician a membrane in the throat, and three hours after the patient's death the following morning, the Board of Health reported a positive culture for diphtheria.

But what I consider of far more importance is the number of procrastinating cases of mild infections in mild diabetics, chiefly in their lower extremities, which frequently prove fatal. The youngest case of sepsis or gangrene of the legs in a diabetic in my personal experience has been fifty years. In other words, these conditions develop at a time of life when diabetes is mild, and why should they so frequently be fatal? Consider with what these mild cases of diabetes have to contend. Handicapped by a lingering infection, which only too often is allowed to continue for months, with kidneys less efficient for throwing off the acidosis attack, deprived of exercise—that recently proven stimulus to sugar consumption (for whoever heard of a poor, old, gangrenous diabetic taking exercise)—these pitiful patients frequently meet a fourth enemy in ether anesthesia; and is it any wonder that a formerly innocent disease becomes virulent and the victim dies of coma? There is no doubt in my mind but that if such cases had been treated vigorously, even with the dietetic methods of a few years ago, a large percentage of the legs amputated might have been saved. In fact, Dr. Stettin has most ably demonstrated this. If one will read his paper it will be seen that his success in these cases was due to two factors: (1) that his patients were given the very best medical treatment of the time, and (2) that they had the advantage of expert surgical care. It is known that if a diabetic patient has gall-stones to be removed he instantly commands the services of the leading surgeon on the senior staff; but if a diabetic patient has a sore toe there is no house officer too young to dress it, until a few weeks later, if the patient survives that long, the surgeon in the amphitheatre amputates the thigh. I recommend to your careful perusal Dr. Stettin's article.<sup>4</sup> Any success that I have had with surgical patients in diabetes has been due to the fact that I know no surgery, and learned that never-to-be-forgotten lesson twenty-one years ago; and, further, that no matter how trivial the ailment I have secured the very best surgical skill for my patients.

4. *Mental Excitement.* An occasional case of coma is precipitated in a severe diabetic by mental excitement. A violent fit of anger in one of the hospital patients, already in a precarious condition, was accompanied by vomiting and inability to retain liquids. Coma soon appeared, and this case I know to have been duplicated by another outside the hospital. A patient with exophthalmic goitre went into coma with far more ease than is the rule.

5. *The Influence of a Fat-Protein Diet or Fat Poisoning.* The explanations of coma thus far given account for many deaths, but by no means for the majority of deaths from coma in diabetes. In these fourteen years at the hospital 9 cases of coma have occurred under my care which could not thus be explained. It is easy to say that the patients die soon after admission, but I cannot get around the thought that if a patient reaches the hospital alive I am responsible for his departure from the hospital alive, too. I will partly excuse myself for the death of one patient five hours after entrance and for a child of two years, who was in coma in ten hours, but I will not plead any excuse for the other 7 deaths. A study of these patients shows none of the factors hitherto mentioned as predisposing to coma, but there is one factor which is common to all, namely, the diet consisted largely of fat and protein with little carbohydrate, or just prior to entrance or after entrance an excessive quantity of fat had been given. Diabetic patients will live untreated for many years without the appearance of coma. They suffer from complication after complication. They are tormented with sepsis, neuritic pains, and pruritus; yet they still live. Their diet is atrocious. Along comes an enthusiastic young doctor—and years ago I could easily have been classed in that group—and presto! change! fat is increased, carbohydrate diminished, and the patient goes into coma. Out of carbohydrate it is impossible to form the acid bodies. When, therefore, carbohydrate is suddenly replaced with fat we deliberately furnish our diabetic patients with material which though it acts partly as a food, acts far more as a poison. At a recent meeting upon acidosis in children, Dr. Jacobi really struck a keynote. He said that prevention is the treatment of acidosis for children, and that those susceptible to acidosis ought not to have fat. What he said for children holds for diabetics. Diabetic patients need fat—it forms the chief constituent of their diet—but they must not be poisoned with it; they must be gradually accustomed to it.

The treatment of acidosis in the past has been unsatisfactory. Like typhoid fever, it should be prevented—not treated—and in uncomplicated cases this can be done. Although 90 per cent. of our diabetic patients will quickly and safely become sugar-free by simple fasting, for the remaining 10 per cent., which would include cases already showing acid poisoning, elderly patients and diabetics with infections, I suggest that prior to giving any fasting treatment a possible acidosis be anticipated by taking away the cause—namely, by the absolute exclusion of fat from the diet, but otherwise make no change in the diet or in the habits of the patient. After two days, or longer if desired, omit protein—another, though lesser contributing factor to acidosis—and thereupon daily halve the carbohydrate hitherto unchanged in the diet, until 10 grams are reached, and then proceed with routine fasting treatment. I would

welcome information as to whether such treatment fails to prevent the appearance of acidosis or to lessen an acidosis already existing. Your aid is solicited, for you must remember that under plain fasting 350 days intervened without a death in the hospital, and if this preliminary treatment to fasting is at all advantageous it will require some time to test its efficacy.

6. *Rapid Loss of Body Fluid.* Vomiting at the onset of coma usually presages death, because the patient is deprived of fluid with which to eliminate acids. Body liquids are so needed that the body in the course of coma becomes obviously dry. This is really only another cause for defective elimination.

But I have been interested for many years in the importance of salt for a diabetic. Recently, too, my attention was drawn by a patient to the fact that in another hospital he lost thirteen pounds during the first four days of fasting treatment. Inquiry developed that he was given, during this period, only water and alcohol. Had he been given broths or some mineral water, suffice it to say that during fasting, even for a week, he would probably have lost little or no weight. This is important, because patients prior to coma frequently lose weight rapidly. Thus in the presence of multiple carbuncles and septicemia one of my patients lost thirty-six pounds in eleven days preceding his death. Years ago in seeking for the cause of edema in a severe diabetic patient who was taking sodium bicarbonate I withdrew sodium chloride from his diet. Prompt loss of weight followed and symptoms of coma appeared. Since then I have been careful not to restrict salt, and I can well understand the opinion of Hodgson, that water rich in salts is really helpful to diabetic patients. On the other hand I would point out that large doses of sodium bicarbonate frequently are detrimental to a patient with threatening coma. How many patients have we had recover who took 20 teaspoonfuls of soda a day and a tablespoonful of whisky every hour and a half? For the last four months not one of my patients has been given a teaspoonful of sodium bicarbonate, and so far I have seen nothing but good results. I prefer to follow Dr. Jacobi's advice and prevent rather than to treat acidosis, and even when it appears I am inclined, though I hold myself ready to change my opinion any moment, to accept the advice of another master of medicine in New York, Prof. Herter, who in 1901 told me he preferred to let his diabetic patients neutralize their acidosis with their own ammonia rather than to give them sodium bicarbonate.

While seeking out the fatal cases of diabetes the number of living patients was ascertained. For comparison I have arranged both groups in decades and completed the average length of life of the fatal cases and the average duration of life of the living cases up to December 1, 1915. It is obvious that among the living cases will be found many in whom the disease is of recent origin, and for



this reason the duration of life of the living cases appears far too low in the table. In another place the living cases will be analyzed more in detail. One of the chief reasons for publishing these statistics which cover the period 1894 to 1916 is the criterion which the table will afford for the estimation of the value of treatment by modern methods.

TABLE II.—DURATION OF LIFE OF 408 FATAL AND 490 LIVING CASES OF DIABETES, DECEMBER 1, 1915.

Age at onset. years.	Number of cases.		Average duration in years.	
	Fatal.	Living.	Fatal.	Living.
0 to 10 . . . . .	33	9	2.06	4.44
11 to 20 . . . . .	48	27	2.79	2.70
21 to 30 . . . . .	40	50	3.30	4.90
31 to 40 . . . . .	53	71	4.43	6.12
41 to 50 . . . . .	71	146	6.08	7.04
51 to 60 . . . . .	97	120	6.63	6.29
61 to 70 . . . . .	52	55	6.00	5.38
71 to 80 . . . . .	14	11	3.71	4.45
81 to 90 . . . . .	0	1	....	0.33

### LINITIS PLASTICA.

BY JOSEPH SAILER, M.D.,

PHILADELPHIA.

LINITIS plastica is a condition in which the wall of the stomach becomes greatly thickened, loses its motility, suffers a marked diminution in its functional activity and as a result leads to death by starvation. The terms of this condition are numerous and all more or less descriptive, leather-bottle stomach, Schrumpf Magen, hypertrophic gastritis (Cruveilhier), chronic indurative sclerosis of the pylorus, cirrhosis of the stomach, linitis plastica (Brinton), fibroid induration, gastric sclerosis are sufficiently indicative of the fact that the wall of the stomach is thickened and hard. Although Cruveilhier and Andral and others had called attention to the existence of this condition earlier, William Brinton was the first to regard it seriously as an independent disease. He devotes a chapter to it in his lecture on "Diseases of the Stomach," and describes two forms, that of contraction and the rarer form of dilatation, and expresses the belief that in a partial form the condition is fairly common, a belief that further experience has not confirmed. He cites no case but must personally have seen several, and for various reasons, given chiefly in a foot note, prefers the name linitis plastica to any other designation. The next important article was that of Hanot, in 1882, who reported one case and analyzed the literature. This was followed in 1893 by the article

of Tilger, who also reported a case and collected all the certain cases previously reported in the literature. His own case occurred in a woman, aged thirty-five years, who had a dilated stomach and an obstruction at the pylorus. An attempt to operate was rather futile on account of the desperate condition of the patient, and she died on the following day. Codivilla collected 23 cases, all of which died and in which the diagnosis was confirmed by autopsy. Of these 13 were men and 10 were women, and the ages ranged pretty regularly from twenty to seventy. He denies very earnestly a carcinomatous nature of the condition. In a postscript he mentions a case reported in which a correct diagnosis was made during life, and digital devulsion twice practised with cure, and Hemmeter, in his text-book, which contains a very excellent article on this subject, reports 2 fatal cases and mentions the fact that he has also seen two others. In 1907 von Sury reported a case from the Pathological Anatomical Institute of the University of Basle with very careful histological study. He defines the condition as follows: (1) a primary more or less extensive increase in the thickness of the wall of the stomach as a result of new-formed connective-tissue, particularly in the submucosa and subserosa; (2) diminution in the volume of the stomach as a result of secondary contraction. This is usually the result of an existing or completed inflammation of the wall of the stomach. He also gives a brief clinical picture of the disease, of which the most interesting features are the frequency of ascites and the fact that a tumor can usually, sooner or later, be felt in the epigastrium. The duration is from three to five years. It occurs in early as well as late life and there are neither metastases nor hematemesis. All these conditions distinguish the condition from carcinoma. The surgical treatment is the most important. He is rather inclined to group it with fibrous polyserositis, either the form described by Pick or the iced liver of Curschmann. One hundred and seventy-two references to the literature, the largest collection hitherto made, are appended to this article. In 1898 Boas reported three characteristic cases of this condition all of which had been cured by gastro-enterostomy. They were all of the obstructive type. It must be admitted that in none of these cases was the subsequent history known for a sufficiently long time to exclude the possibility of a carcinomatous change. Quenu, in 1908, reported 2 cases of gastrectomy for this condition. The man lived two years and then died of hemorrhagic pleurisy, probably carcinomatous. The woman lived two and a half years and died of a local return. In both cases the histological examination indicated the carcinomatous nature of the process. Munter in discussing four cases of this condition reached a conclusion that there are several forms of chronic gastritis. These forms are first linitis plastica. This is characterized by marked thickening of the gastric wall due to proliferation of the connective-tissue.

Thickening usually begins at the pylorus and leads gradually to contraction with partial stenosis and possibly in the end, if the patient survives long enough, to complete stenosis. There is some tendency to the formation of adhesions to the surrounding organs, and in all probability the lymph glands adjacent to the stomach frequently become enlarged, but there is no tendency to metastases. The cachexia is solely due to starvation, and the prognosis appears to be favorable if the obstruction is relieved by gastro-enterostomy. Curiously enough there is good reason now to suppose that after the gastro-enterostomy some degree of retrograde change takes place and the stomach to a certain extent returns to a normal condition. Second, a diffuse carcinoma of the wall. For some reason that is not rendered clear by a study of the literature it seems to be the opinion of many surgeons that this is the only type of the disease. It is unfortunate that this should be so, as it leads to a pessimistic prognosis which is invariably justified if no operative interference is undertaken. This is characterized by thickness of the wall, the histological picture of which is probably not greatly unlike that of pure linitis. I have had the opportunity of studying one case of carcinomatous linitis gastrica. At least I was under the impression at the time that this was the correct diagnosis. The patient, a negro, was brought to my service at the Polyclinic Hospital some years ago with symptoms of obstruction at the cardia. This was diagnosed carcinoma without definite proof, and gastrostomy was advised. The wall of the stomach was found thick and leathery. Nevertheless, Dr. John B. Roberts succeeded in making a satisfactory gastric fistula through which the patient was fed, and he gained weight. The power of swallowing through the esophagus returned, and the patient, who was a caterer, left the hospital and indulged his appetite pretty freely. He was brought back forty-eight hours after his discharge suffering with the symptoms of peritonitis, to which he succumbed in a very short time. No autopsy was permitted. The clinical picture of carcinomatous sclerotic gastritis and linitis plastica does not differ in the beginning. There is no satisfactory way of making a differential diagnosis excepting by an incision and histological study of portions of the gastric wall, and for reasons that I shall consider later, even this may be unsatisfactory. The real differentiation is made not by the more rapid course and greater cachexia, because these after all are quantitative and untrustworthy, but by the occurrence of carcinomatous metastases to other organs, particularly the liver.

The third condition is syphilis. If the other signs of sclerotic gastritis are present and the patient has a positive Wassermann reaction it is justifiable to use antisyphilitic medication actively with the hope of benefiting the condition. As far as I know there are no cases on record of this type of the disease that have actually been cured by antisyphilitic treatment. Finally, it has been sug-

gested that chronic sclerotic gastritis may be a part manifestation of a multiple serositis. These are probably cases characterized by ascites that rapidly reaccumulate, and it is doubtful whether the gastric symptoms ever become very definite. In the only one case of this kind that I saw, a young man, aged twenty-seven years, who had obliterative pericarditis, chronic pleuritis with reaccumulation of pleural fluid and chronic ascites with rapid accumulation of ascitic fluid, the gastric wall was found greatly thickened. At the autopsy this thickening was found to be due to a curious hyaline change in the serous membrane similar to that found over the lung, liver, and spleen, but there had been no gastric symptoms of importance during the brief course of the disease.

The prognosis without treatment is hopeless. No medical treatment is known. Therefore the only hope lies in some efficient form of surgical interference. In 1908 von Eiselsberg reported a case upon which he had operated in 1902. The patient, a woman, aged forty-one years, had been ill for about three years with vomiting and loss of weight. At the first operation the stomach was found to be thickened and adherent to the surrounding tissues. Nothing was done excepting to free a few adhesions. At the second operation a jejunostomy by the Witzel method was performed. For one year she was fed almost exclusively through the fistula with liquid food. She regained her former weight of 72 kgms. Later she increased still more in weight and was able to take a certain amount of food by the mouth. Six years after operation she was still in good health, had married again, and weighed more than at any time before the operation.

The direct diagnosis depends (1) upon the clinical signs, (2) on the  $x$ -ray findings, and (3) on a possible exploratory laparotomy. None of the clinical signs are really characteristic, and upon them alone I do not believe that a positive diagnosis can be made. A diagnosis can be surmised, however, if the symptoms develop gradually; if there is evidence of decreasing capacity of the stomach, which might occur also in hour-glass stomach; if there is fulness and perhaps a firm, rounded mass in the epigastrium; if there is vomiting that often depends upon the character of the food ingested, so that the patient can often predict when it is likely to occur. These things may lead to a suspicion of a contracting wall. The  $x$ -ray picture is usually characteristic. The small irregular lumen, the irregularities remaining constant in successive pictures; the contraction of the lower portion, the expansion of the fundus and, as occasionally seems to happen, the permanently patulous pylorus with a rapid flow of bismuth into the intestines, all point to this one condition. I have recently seen, however, a patient whose  $x$ -ray pictures seemed to present most of these features, and yet at an operation nodular sarcomatous thickenings were found in the gastric wall. The results obtained from exploratory laparotomy

are, of course, decisive. If there are adhesions between the stomach and surrounding structures it is only important to recollect that in the absence of metastases a diagnosis of carcinoma can not be made with certainty.

Souper has recently reported an interesting case correctly diagnosed, that was of the form associated with stenosis of the pylorus, and the patient three years after the operation of gastro-enterostomy was apparently perfectly well. As Souper very sensibly remarks, the possibility of carcinoma is probably not to be considered now. Dr. David Riesman recently reported a case, as yet unpublished, before the Musser Clinical Club, and the patient is still alive and in good health five years after a gastro-enterostomy. It seems to me clear, therefore, that not all of these cases can be carcinomatous, although the two cases of Quenu suggest that at least some of them are, and in this state of uncertainty it is important to treat every case as if it were benign. Bland-Sutton, in a recent excellent article on this subject, is somewhat undecided in his views and inclined to think that many of the cases are not malignant in nature. To my mind one of the most difficult tasks in morbid histology is the differentiation of a chronic sclerosing inflammation of the mucous membrane from carcinoma. The pictures presented by the two conditions are often similar to a puzzling degree, and I should be loath to reply upon the histological evidence of the stomach wall alone, unsupported by demonstrated epithelial metastases to the lymph glands or other organs.

The following case came under my observation and an opportunity was presented to make careful studies:

The patient is white, aged forty-six years, a physician. His previous history is unimportant. He has been successful in his professional work. Has been very fond of outdoor life, particularly as a hunter of big game, in the pursuit of which he has spent many weeks at a time. He has indulged moderately in alcohol and tobacco. On June 1, 1913, he was operated upon for bilateral hernia. The operation was entirely successful, the wound healed by first intention, but for some days following the operation there was intense pain in both groins. In July he noticed distinct loss of weight and suffered from pain immediately after eating, that frequently was associated with nausea. To relieve both the pain and the nausea he resorted to voluntary vomiting. In May, 1913, he weighed 178 pounds, approximately his weight for the previous ten years. In December of the same year he weighed 160 pounds. The physical examination at this time was practically negative. The thoracic organs were normal. The abdominal walls were well relaxed, facilitating palpation, but aside from the descending colon no organs were felt. There were no areas of tenderness. Loud gurgling was produced by pressure in the epigastrium. Deep pressure just above the umbilicus was slightly uncomfortable. There was no splash

in the stomach two hours after taking food (glass of milk). By auscultatory precussion the greater curvature of the stomach appeared to be at the level of the umbilicus. The nervous system was normal. An examination of the blood showed a moderate degree of anemia, 7000 white cells and a normal differential count. The blood-pressure, 116 and 84, was slightly below normal. The gastric contents showed no free hydrochloric acid and a total acidity



FIG. 1

of 38; no occult blood; a very large amount of mucus; no Oppel-Boas bacilli; no lactic acid. There was definite evidence of peptic digestion in the diluted contents by Mettè's method. The urine was normal. A diagnosis was made of severe catarrhal gastritis, the patient placed upon a careful diet and given daily lavage. This produced great subjective improvement for ten days. Then he complained of a crawling sensation in the stomach, with nausea and

pain after eating. His weight had decreased four pounds. At this time the gastric contents obtained two hours after a mixed test breakfast gave a total acidity of 46; no free hydrochloric acid. Peptic digestion was present when the contents had been diluted with  $\frac{1}{2}$  normal hydrochloric acid solution. There was no occult blood; no lactic acid; no Oppler-Boas bacilli; no sarcinae, but a great deal of squamous epithelium. During this time the patient



FIG. 2

had been on hydrochloric acid, but the last examination still failed to give free hydrochloric acid, although the total acidity had risen to 68. There was no evidence of proteid digestion and no peptic activity in the filtered stomach contents, but when diluted with  $\frac{1}{2}$  normal hydrochloric acid in proportion to 1 to 16, proteid digestion was fairly active. In this specimen for the first time a large amount of pus was observed. Numerous attempts were made to obtain

test meals, only a few of which were successful, because the stomach emptied itself so rapidly. All gave practically the same result excepting the variation in the amount of total acidity. Pus was constantly present. Occult blood never. Very often even fifteen minutes after the ingestion of food the tube failed to obtain any of the gastric contents. An attempt was made with an Einhorn tube on two occasions to obtain duodenal contents, but if they were obtained they corresponded in all respects to the gastric contents, and nothing was learned excepting that in the supposed duodenal contents trypsin and bile could not be demonstrated. Early in January, Dr. Miller, of the German Hospital, took two x-rays that were clear and definite (see Figs. 1 and 2). They showed that the lumen of the stomach was very much reduced in size, was distinctly irregular in outline, and a diagnosis of linitis plastica was made. Subsequently fluoroscopic studies were made by Dr. H. K. Pancoast at the University Hospital. These confirmed the findings of Dr. Miller, indicating greatly thickened gastric walls, and in the fluoroscope a most extraordinary rapidity of the gastric emptying was observed. This was not hypermotility due to excessive peristalsis, but rather to the fact that the bismuth flowed almost immediately through the rigid tube formed by the thickened stomach walls into the duodenum. The patient lost weight for a time until he reached a minimum of 139 net. Later assimilation seemed to improve, and at one time his weight increased to 149 pounds, but averaged approximately 145 pounds. There was otherwise no change in his condition, excepting that from time to time some tenderness could be obtained just to the right of the median line near the costal margin, and occasionally a mass could be felt which seemed to correspond to the rounded greater curvature of the stomach. This could be felt on deep inspiration and was not constantly present. In view of the pus it was suspected that some infectious process might be present in the wall of the stomach, and Dr. Damon R. Pfeiffer performed a series of agglutination tests with all the microorganisms that he happened to have in the pathological laboratory of the German Hospital, amounting to about twenty. These included all the ordinary pyogenic organisms, colon, typhoid, and various other strains of paratyphoid, but all were negative. Several hypodermic injections of theosinamin were made without definite result, although the patient complained of a distinct sensation in the region of the stomach, and also, somewhat unexpectedly, in the hernial operation wounds, immediately after the injection. There was no evidence of improvement, and they were discontinued. It was therefore decided to perform an exploratory operation, which had not been done earlier, partly because there was no evidence of obstruction in the gastro-intestinal tract and partly because the surgeon consultants had advised against it. However, they were persuaded. The operation was merely an inspection of the



abdominal viscera, which confirmed the clinical diagnosis, and the abdomen was then closed. The surgeons were very positive that the condition was cancerous. There was, however, in spite of careful search, no evidence of metastasis. There were no enlarged glands along the lesser curvature, but some masses were found around the greater curvature that were probably enlarged lymph glands. There were some very slight adhesions around the pylorus, which were separated, and the great omentum was adherent to the wall of the abdomen, apparently close to the sites of the operations for hernia. The patient made a prompt and satisfactory recovery from the operation. Six months later his condition had distinctly deteriorated. For a time he had felt better and had been able to eat nearly everything. His strength increased, although his weight did not go above 140 pounds. He was able to take long walks and even to go on shooting expeditions. Then after about five months he noticed that liquid food could not be taken with comfort, and this applied also to soft food such as fruit, light desserts, etc. There was a good deal of nausea and almost complete anorexia. His weight steadily decreased to about 132 pounds. He appeared cachectic and was incapable of much exertion without great fatigue. The physical examination showed only a more distinctly palpable mass in the epigastrium extending under the right rib. The x-rays showed distinct contraction of the lower portion of the stomach, the lumen was greatly reduced, and the thickness of the wall not very much increased. The condition appeared to be exceedingly desperate, and it was resolved to attempt a second operation with the idea that if a gastro-enterostomy could not be performed, and it was not our expectation that it could, at least a jejunostomy could be attempted in a hope that the brilliant results obtained by von Eiselsberg in his case would be reproduced. Dr. Finney, of Johns Hopkins, was consulted, and he believed that in view of the apparent hopelessness of the condition unless something were done, it would be worth while to make a trial. The patient accordingly went to Baltimore, and in October, 1914, Dr. Finney reopened the abdomen. He found that the stomach was hard, contracted, and bound by firm adhesions to all the surrounding tissues, so that it was quite impossible to consider any operation upon it. He accordingly performed a jejunostomy by the Witzel method. After the operation the patient vomited almost constantly. Very little food could be given by the tube and some of it returned through the wound. He rapidly lost weight and strength until he became a mere skeleton, and about three weeks after the operation died. An autopsy was performed by Dr. Damon R. Pfeiffer. His notes are as follows:

The body was much emaciated and the abdomen scaphoid. An incision was present in the upper right rectus muscle, about 12 cm. in length, which was healed except near the lower extremity, where the sinus created by a jejunostomy tube was still open. The body had been embalmed.

On section the thoracic viscera presented no abnormalities. On opening the abdomen, numerous dense adhesions were found binding the jejunum, pyloric portion of the stomach, and adjacent gastrocolic omentum to the abdominal wall. These were apparently inflammatory, the result of operation. Freeing the stomach, it was found in its usual position, high up beneath the left diaphragmatic arch, but extremely narrowed throughout its entirety, and very dense and firm. On removal and opening for examination it was found that the entire wall was diffusely thickened, varying from approximately 1 to 2 cm. in thickness. On the greater curvature, about 6 cm. from the pylorus, an ulcerated area, about 2.5 cm. in diameter, was present, with thickened precipitous edges. The mucosa throughout was loosely attached to the thickened wall and was thrown up in large rugæ. The thickening stopped abruptly at the pyloric ring. The pylorus itself was patulous but not distensible, except with difficulty. The peritoneal surface of the stomach was smooth, except where inflammatory adhesions had been present, and in the neighborhood of the ulcerated area, where a number of small nodules, mucoid in appearance, were attached to the stomach both on the greater and lesser curvatures. The omenta in this situation were thickened and contained a number of lymph nodes, varying in size up to 1 cm. in diameter.

The liver was atrophic but otherwise normal in appearance, except for cholecystic adhesions the bile passages were free and normal. The pancreas showed no abnormality, but in the peripancreatic and peri-aortic tissues of the neighborhood a few moderately enlarged lymph nodes were present.

The remaining abdominal viscera were normal in gross appearance.

Microscopically the edge of the ulcer showed on its gastric surface, an enormous hyperplasia of tubular glands, which correspond in appearance rather closely to the glandulæ gastricae. They are, however, more closely set, without the usual intervening stroma and the lining cells are much larger and of the mucoid type. In some areas they are quite irregular and are undergoing mucoid degeneration *en masse*. In certain areas the appearance strongly suggests that of "Brunner's glands." That the invasive tendency is relatively slight is shown by the fact that this hyperplastic epithelial mass is quite well circumscribed from the underlying fibromuscular stomach wall, though in many places a distinct basement membrane is absent. In other places distinct evidence of invasion is seen.

The submucosa is not distinct from the muscularis with which it merges as a dense thickened fibromuscular layer. Here and there in the intermuscular spaces, apparently corresponding to the lymphatics are found strands and clumps of cells, evidently derived from the epithelium of the growth above described. There is no evidence that the ulceration was a primary condition with secondary

carcinomatous implantation, on the contrary the ulceration appears to result from degeneration of the hyperplastic epithelial mass. The invading cells within the fibromuscular layer occasionally reproduce a tubule; but for the most part they exist as simple strands without definite arrangement. They can be observed moreover in all stages of degeneration. Apparently, either by reason of compression by the surrounding tissue, or as a result of essential biological characteristics the individual cells show a marked tendency to undergo mucoid degeneration and necrosis. Where the cells are enclosed by dense fibromuscular tissue they tend to disappear completely, but where no surrounding pressure is exerted, as on the exterior of the stomach or in the lesser omental tissues as hereafter noted, their disappearance results in the deposit of considerable masses of mucoid material. That these masses are the result of degeneration of the cell bodies themselves can be inferred by the presence of cells in all stages of degeneration and fusion with the mucoid material.

Sections from the thickened gastric wall at various points, distal and proximal to the ulcerated area, show with only minor variations the same process. The obvious interpretation of this growth and the excessive thickening of the gastric wall is as follows: The greater curvature is the seat of the primary colloid or mucoid carcinoma which possesses invasive characteristics with low cellular vitality. Infiltration takes place along the tissue planes permeating the lymphatics of the entire stomach. As a result of degenerative processes the invading cells tend to undergo mucoid change and death. It seems possible that the presence of this cellular infiltrate and its products result in a hyperplasia of the muscular and fibrous tissue of the stomach, thus explaining the thickening of the wall. That a functional hypertrophy is not the cause of this thickening is shown by the fact that it is as great distal to the primary ulcerated area as proximal to it.

Section through the gastrohepatic omentum adjacent to the nodular area shows marked infiltration with a growth of the typical mucoid character. Sections from adjacent lymph nodes in the gastrohepatic and gastrocolicomenta also show in some instances infiltration with the typical cells of the growth. One small peri-aortic node from the region of the celiac plexus 0.5 cm. in diameter presents a similar infiltration. In the lymph nodes the globular cells lie closely in the marginal sinuses and central lymph spaces, and show the same degenerative tendencies but without the permanent deposit of mucoid material.

The pancreas and remaining intra-abdominal organs show no noteworthy abnormalities and no evidence of metastatic nodules. Noteworthy features are: (1) The suggestion of a derivation of the growth from Brunner's glands; (2) the evidence of diffuse infiltration of the stomach wall by the growth, with its pronounced

degenerative tendencies and the probable irritative hyperplasia of the fibromuscular coats; (3) the distinct evidence of extragastric lymphatic extension, which, however, in view of the duration of the condition, must be regarded as a late or exceedingly slow process.

The interesting features of this case appear to be as follows:

1. The development of symptoms one month after the operation for hernia raises the question whether the latter could have had anything to do with the subsequent gastric condition. If it had there is no possible way of demonstrating the fact. There was not at the time nor at the subsequent operation aside from the omental adhesions any evidence of infection of the hernial wounds.

2. The persistent patulous condition of the pylorus is unusual for, with one exception, in all cases hitherto recorded obstruction and retention of the gastric contents has been present.

3. The persistent absence of free hydrochloric acid, even though the total acidity sometimes reached 68, is somewhat difficult to explain.

4. The fact that pepsin was undoubtedly secreted, although, in the absence of free hydrochloric acid, it did not act upon proteids, but it always became active as soon as the gastric contents were diluted with hydrochloric acid solution. Pus was frequently found at first; occult or visible blood never; lactic acid never in this case, and although it has been observed in some of the recorded cases, it is not constant and probably only occurs when there is stagnation of the gastric contents.

5. The evidence at the time of operation that the process had begun in the pyloric region. The wall in this region was distinctly thicker, somewhat harder and appeared more altered than the remaining portion of the stomach, although the thickening of the gastric wall extended as far as the fundus.

6. The distinct evidence of improvement that occurred twice during the course of the disease, once when the patient gained ten pounds in weight and the other time when he became so much stronger that he was able to undertake a considerable degree of out door exercise walking as much as four or five miles across country almost daily. Why this improvement occurred in view of the progressive nature of the process it is difficult to understand.

The treatment of this condition must of necessity be purely surgical, and it seems in view of several cases that have been reported in which either temporary improvement or even apparently a cure occurred, that, in the absence of a positive Wassermann, operation should be undertaken as soon as the diagnosis has been made. If the process is carcinomatous it may in the early stage be possible at least to attempt a gastro-enterostomy. If it is a sclerotic inflammation secondary to an ulcer a gastro-enterostomy offers considerable hope for permanent relief, as in the cases of Souper and Riesman. If neither of these operations can be attempted it

is possible that a jejunostomy may result as successfully as did that of von Eiselsberg. Of course, if the process is merely a part of a multiple serositis nothing can be done, but the patient will probably not suffer seriously from the exploration.

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## CLINICAL STUDY OF PAIN ARISING FROM DIAPHRAGMATIC PLEURISY AND SUBPHRENIC INFLAMMATION.<sup>1</sup>

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IN 1911 we reported the results of some experiments on the occurrence and distribution of pain, where the pleural membranes were irritated during the process of removing fluid from the cavity.<sup>2</sup>

We found that the visceral pleura is not sensitive to pressure or scratching of a wire. We found that irritation of the parietal pleura nearly always produced pain, sharp and localized over the area irritated and never referred to distant parts, *e. g.*, the neck and abdomen.

We found that irritation of the diaphragmatic pleura over the outer margin set up pain in the hypochondrium and often in the abdominal wall down to as far as the navel or even to the groin, while over the central portion of the diaphragm it caused pain in the neck, particularly along the trapezius muscle ridge.

From these experiments it seemed justifiable to conclude that

<sup>1</sup> Read at the meeting of the Association of American Physicians at Washington, D. C., May, 1915.

<sup>2</sup> An Experimental Study of the Pain Sense in the Pleural Membranes, *Arch. Int. Med.*, December, 1911, vol. viii, No. 6, p. 717.

the marginal part of the diaphragmatic pleura receives its sensory supply from the lower six intercostal nerves and that the referred pain is attributable to an irritation of the corresponding sensory segments of the spinal cord, which endow the abdominal wall with sensation.

Also that the central portion of the diaphragm receives its sensory nerves from the phrenic nerve, which carries afferent impulses to the cervical cord, and sets up reflex pain in the corresponding spinal segments, namely, the third and fourth cervical.

To supplement these experiments we have observed the character and location of pain in a series of clinical cases in which there was inflammation of the serous membranes lining the upper and lower surfaces of the diaphragm.

ANALYSIS OF SIXTY-ONE CASES OF DIAPHRAGMATIC PLEURISY. During a six-year period sixty-one cases of diaphragmatic pleurisy have been seen and examined by the writer. Such a collection would have been impossible had it not been for the interest and courtesy of the internes and staff of the Cook County Hospital.

Twenty-nine of the cases had a lower lobe pneumonia with associated pleurisy, the remaining thirty-two had pleurisy alone.

Thirty-nine were situated on the right side, twenty-one on the left and one was bilateral. The diagnosis was in most instances made evident by physical findings in the thorax, in four instances confirmed by autopsy, and in six instances abdominal disease was excluded by exploratory laparotomy.

*Pain* referred to parts distant from the seat of inflammation was the outstanding symptom of these cases. *Referred abdominal pain* was present in fifty-four cases, in all cases involving the upper quadrant (7 to 10 dorsal segments), and in twenty-five cases the lower quadrant as well (7 to 12 dorsal segments). Bilateral pain in the belly was noted four times.

The pain was usually spontaneous and with it was tenderness to pressure. *Hyperesthesia* and *hyperalgesia* of the skin were almost constant and showed a decided tendency to follow band-like areas, corresponding to different spinal segments. Over this sensitive area the *musculocutaneous* reflexes were exaggerated and often the wall remained in a state of rigidity.

The *maximum points of pain* and tenderness to pressure were especially studied. (Fig. 1.)

This point was located:

- (a) In the gall-bladder region, 10 times.
- (b) Lateral to and slightly above the navel, 15 times.
- (c) Near McBurney's point, 2 times.
- (d) Over the navel, 1 time.
- (e) Midpigastrium, 1 time.
- (f) Splenic region, 1 time.
- (g) Lumbar region, 2 times.

*Referred neck pain* occurred in thirty-three cases, or in a little more than one-half of the total. The pain was located by the great majority of patients along the trapezius ridge, occasionally over the shoulder cap and in the supraclavicular space. These areas all are supplied with sensory nerves by the third and fourth cervical spinal segments.

The pain was usually spontaneous and of a sharp stabbing character, always well localized by the patient with the tip of his finger. Pressure over this point was often very painful. The skin and subcutaneous tissues in the immediate neighborhood showed the same hyperalgesia and hyperesthesia as were found over the abdomen, but the point of maximum pain and tenderness in the neck was sharply localized, and more constant.

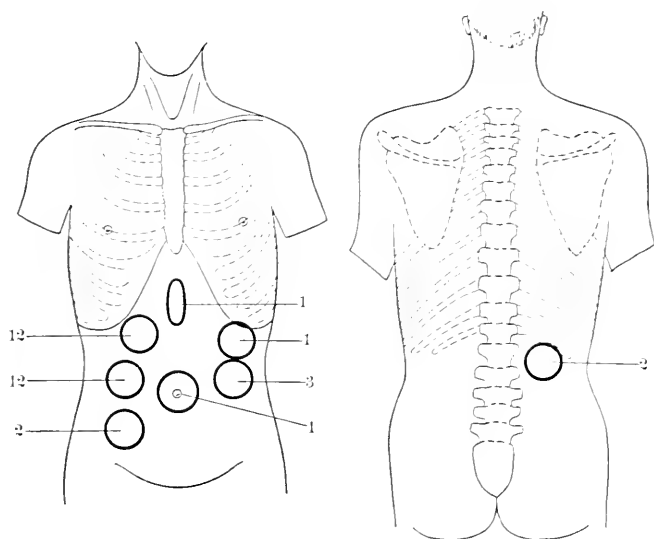


FIG. 1.—Points of maximum pain and tenderness in abdomen and back occurring in 61 cases of diaphragmatic pleurisy.

The exact locations of maximum pain points are illustrated in Fig. 2.

**FACTORS INFLUENCING PAIN.** The appearance of referred pains in the abdomen or neck was generally early in the course of the disease. More often abdominal pain preceded the neck pain when both were present. The *duration* of the pain and tenderness varied in much the same way as in parietal pleurisy. Sometimes the pain disappeared after a few hours; as a rule it persisted for one to three days and occasionally for over a week.

The pain was nearly always induced or aggravated by cough and deep inspiration, especially during the acute stage.

Measures limiting the excursion of the diaphragm on the affected side, such as lying on the painful side or tight pressure of an abdominal band often gave relief. Some patients secured ease by lying doubled up on the affected side with the shoulder held down by a pillow.

**SPECIAL FEATURES.** The abdominal pain was associated with a maximum point of pain and tenderness far more frequently on the right than on the left side. Such a point was observed in 25 out of 36 cases on the right side or 70 per cent.; while it was noted in only 7 of 18 cases on the left side, or 40 per cent.

In contrast to this disparity, the neck pain occurred with almost equal frequency on the two sides. *Tenderness of the phrenic nerve,*

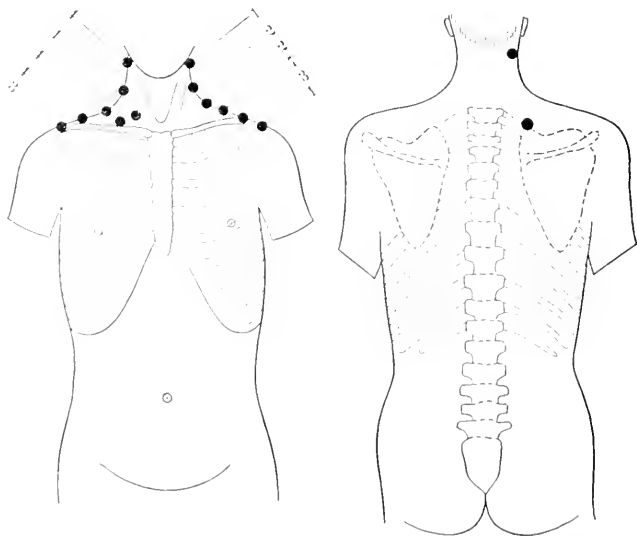


FIG. 2. Points of maximum pain and tenderness in the neck region occurring in 61 cases of diaphragmatic pleurisy.

a symptom emphasized by many writers was found in but one case and that was doubtful. *Vomiting* was present in 10 cases and was often responsible for a mistaken diagnosis of abdominal inflammation. *Hiccough* another symptom supposed to be common in diaphragmatic pleurisy, was noted in only 5 cases, being unusually severe, however, in three.

**DOES THE REFERRED PAIN ORIGINATE IN THE LUNG OR PLEURA?** Head, Russell, and others have held that the irritation comes from the lungs, as they question the capability of the pleura to give rise to referred pain. In our series pneumonia of the lower lobe was present with pleurisy in twenty-nine cases. In thirty-two cases pleurisy was present without any signs of consolidation. This



indicates that the pleura over the diaphragm does cause referred pain and casts doubt upon the ability of the lung itself to do so. The pleural origin of referred pain is further corroborated by our experiments<sup>3</sup> in which irritation of the lung set up no pain, whereas, irritation of the diaphragmatic pleura gave rise to referred abdominal and neck pain.

**MISTAKEN DIAGNOSES IN DIAPHRAGMATIC PLEURISIES.** *Appendicitis* was incorrectly diagnosed in 9 cases. Two of these were operated upon and the abdominal viscera found to be normal.

*Cholecystitis* was diagnosed in 6 instances, 2 of which came to laparotomy without discovering any pathological condition of the gall-bladder or the neighboring structures.

*Ulcer of the stomach* with perforation was twice diagnosed and once operated upon without discovering any lesion in the belly.

*Liver abscess* was diagnosed in two patients. One was opened up with negative results. The other mistaken diagnoses included one instance each of *peritonitis*, *renal calculus*, *infectious lumbago*, and *brachial neuritis*.

Several of the above-mentioned patients were prepared for operation but were saved by the conservatism of the surgeon. I believe the unusual interest in referred abdominal pain awakened by frequent discussion of the subject by the Staff of the Cook County Hospital has saved from needless operation many cases that in former years would have been promptly submitted to exploration.

**DIFFERENTIATION OF PAIN IN DIAPHRAGMATIC PLEURISY AND IN INFLAMMATION OF ABDOMINAL VISCERA.** Our knowledge of visceral pain has been so enriched by physiological investigators, more particularly by Hilton, Ross, MacKenzie, Head, Meltzer, Lenander and Hertz, that we should interpret our clinical findings in the light of their results. Without discussing their work in detail, we may recall that Lenander and MacKenzie have maintained that the viscera are insensitive to pain, since during operations under cocaine the stomach, intestine, appendix, gall-bladder, and other organs may be cut, burned, and scratched without producing any painful sensation. All pain proceeding from abdominal inflammation they believe arises from irritation of or traction on the parietal peritoneum, which is supplied with spinal nerve fibers that are specially designed to carry pain stimuli to the cord and brain. The sympathetic nerve fibers supplying the viscera, they say, do not have the power to carry painful stimuli.

These conclusions must be modified by the observations of Kast and Meltzer, who found that the sensibility of the viscera during such operations is appreciably lessened both by the general toxic effect of cocaine and by exposure to the air.

It has been pointed out by numerous investigators that the

<sup>3</sup> Loc. cit.

viscera may be insensitive to the ordinary painful stimuli such as cutting and burning and yet be sensitive to the "adequate stimulus." The adequate stimulus for all the hollow viscera seems to be *tension*. As a result of tension the pain of colic may be explained.

The theory that generally prevails today is that proposed by Ross and supported in essentials by Head, viz., that there are two distinct types of pain in visceral inflammation.

1. *The splanchnic or visceral pain*, which is conveyed directly to the cord and brain by the splanchnic nerves. This pain is, as a rule, dull and deep. A good illustration of this pain is seen in pressure on the testicle or over an inflamed ovary, appendix, or gall-bladder. As a rule, it is localized near the site of its origin.

2. *Somatic or referred pain* is usually located at some distance from the seat of inflammation. It is produced when afferent stimuli from the viscera travel along the splanchnic nerves to the posterior roots of the cord, where they so irritate the corresponding spinal somatic nerves that they give rise to pain in the area of skin and muscles supplied by these nerves.

This pain has a band-like distribution over the trunk and an irregular distribution over the neck, head, and extremities. The pain is in the skin, subcutaneous tissues and muscles and therefore superficial. The sensitized area is hyperesthetic, hyperalgesic and often characterized by painful tender points. The muscular cutaneous reflexes are exaggerated. When the parietal peritoneum is involved then there is direct irritation of the spinal somatic nerve which is similar in kind to referred pain along the same nerves. It is reasonable to expect that both types of visceral and referred pain may be present in visceral inflammation. But clinical experience seems to show that the visceral pain is more constant in abdominal affections than the referred, also that visceral pain may occur alone, *e. g.*, in intestinal colic and some cases of catarrhal appendicitis. Referred pain from the diaphragmatic pleurisy renders painful the spinal nerves supplying the abdominal wall, but the deep visceral pain is not present. Steady deep pressure over the appendix or gall-bladder is well tolerated, whereas in inflammation of these organs deep pressure gives rise to severe deep-seated pain.

The main points of differentiation between diaphragmatic pleurisy and inflammation of the abdominal viscera are as follows:

1. The skin and muscles of the abdomen are more sensitive to pain and touch in referred pleural pain than in visceral disease. This is best elicited by pinching of the wall and scratching of the skin.

2. The cutaneous reflexes are more lively in referred pain than in visceral disease as a rule.

3. Deep pressure with the flat surface of the fingers is well borne in referred diaphragmatic pleural pain, while it elicits a dull, deep

pain when applied over an inflamed organ, *e. g.*, an appendix or gall-bladder.

4. Evidences of respiratory infection are usually present in diaphragmatic pleurisy, such as cough, expectoration, herpes of lips, sore throat, high leukocytosis, rapid respiration, etc.

5. Appearance of a sharp, definitely localized pain in the neck on the same side as the abdominal pain often reveals the true condition, since it points to irritation of the phrenic nerve.

6. The referred pains in the neck and abdomen are usually induced or aggravated by cough and deep inspiration.

7. Nausea and vomiting are more constant in visceral abdominal inflammation, but may occur and be very pronounced also in diaphragmatic pleurisy.

8. Hiccough is not a common symptom in diaphragmatic pleurisy, contrary to the current belief. It was present only five times in our series of sixty-one cases. It is more often seen in visceral diseases of the abdomen than in diaphragmatic pleurisy.

**SUBPHRENIC INFLAMMATION.** In the study of pain distribution from subphrenic inflammation, we are greatly handicapped. The opportunities for experimental irritation of the under surface of the diaphragm in human beings are rare. Moreover, the existence of abdominal pain in the course of subphrenic inflammation may be properly attributed to associated inflammation of the abdominal viscera. Only in those cases in which definite, sharply localized pain and tenderness develop in the neck or shoulder region, can we be sure that the diaphragm is involved. We have collected six cases of subphrenic inflammation exhibiting neck pain, three on the left side and three on the right. The painful point is in every respect identical with the referred pain in diaphragmatic pleurisy.

The nerve supply of the peritoneal covering of the diaphragm is probably the same as that of the pleural surface, that is to say, the lower intercostal nerves supply the outer margin, and the phrenic nerves supply the central portion. Hence it is impossible to differentiate between supraphrenic and subphrenic inflammation by the pain alone. The symptomatology and physical findings must also be considered, in order to establish the diagnosis.

## THE CEREBRAL NERVE DISTURBANCES IN EXOPHTHALMIC GOITRE.

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THE cerebral disturbances which occur in exophthalmic goitre are among the rarer manifestations of this remarkable disease. Headache, often intense, is a very common symptom, as are

irritability, emotional outbursts, and disturbances in sleep with terrifying dreams. Graver associated conditions may occur, such as neurasthenia, hysteria, and the various psychoses, such as manic-depressive insanity, melancholia, dementia precox, paranoia, and acute delirium. Organic cerebral changes giving rise to convulsions, epilepsy, and epileptiform attacks, muscular weakness, paralyses of the cerebral nerves, hemiplegias and paraplegias, anesthesias, paresthesias, and hyperesthesias may be associated with this disease.

The chief purpose of this communication is to call attention to one group of these cerebral disturbances, namely, the cerebral nerve palsies. In the enormous literature on Basedow's disease not more than eighty cases, including all types, are recorded, the great majority of which have been observed in European clinics. Only four cases appear in American literature (Campbell Posey, Dana, Gordon, Bartholow). At the Johns Hopkins Hospital, among more than 300 cases of exophthalmic goitre occurring in the service of Dr. Halsted, the case to be reported is, with the exception of an occasional mild grade of ptosis, the first instance which has come under observation.

The cerebral nerves affected are most commonly those controlling the movements of the eyes and lids, but a review of the literature shows that almost every cerebral nerve has been involved, either alone or in combination with other nerves. Least common is the group of cases with an associated bulbar paralysis, of which perhaps only ten have been reported. The case to be described is of this group.

The patient, a Russian Jew, aged twenty-three years, a recent graduate in medicine, was admitted to the surgical service of the Johns Hopkins Hospital January 31, 1911, complaining of weakness, vomiting, shortness of breath, difficulty in swallowing, and double vision. The family history is unimportant. The mother is in rather poor health and nervous. There is no history of exophthalmic goitre in other members of the family. The patient has always been delicate and of a nervous temperament, but has not had any severe illnesses. He was admitted to the medical service of the Johns Hopkins Hospital December 17, 1907, complaining of weakness and vomiting. The history which he gave at that time was as follows:

Two years before (in 1905) he had an attack of vomiting lasting for a few days; a year later he had a second similar attack; the third attack (for which he was admitted to the medical service) had been of two months' duration, and had increased in severity so that even small amounts of milk could not be retained. He had lost thirteen pounds in weight in the week immediately preceding his first admission. The vomiting had not been associated with nausea or pain; the food ingested was expelled without effort

or distress. During the few days before admission he had had diarrhea, four to five movements daily. Examination at that time (in 1907) showed an emotional, nervous young man with normal pulse and temperature; no exophthalmos or characteristic eye signs, apparently no enlargement of the thyroid gland, and no cerebral nerve disturbances. The lungs were clear; there was a faint systolic blow at the apex of the heart; the abdomen was negative. Acetone and diacetic acid were present in the urine. Dr. Barker noted, at this time, pigmentation of the skin and the absence of axillary hair. The patient remained in the hospital but two days, at the end of which time he insisted upon going home.

*Present Illness* (January 31, 1911). The patient states that he was perfectly well until March or April, 1909. He then noticed a swelling of his neck, which at first was not accompanied by any symptoms. Just previous to its appearance he had been roughly handled by his fellow-students and badly frightened. The enlargement of the neck was very rapid. Three months after the first appearance of the goitre he was unable to wear a collar, and had become very nervous. Tachycardia was first noted several months after the appearance of the goitre, and has persisted, but without subjective palpitation of the heart. A year after the appearance of the goitre (1910) he became aware of a droop of the right upper lid; there followed soon a similar condition of the left lid. This bilateral ptosis has gradually become more marked, and at present the patient is quite unable to raise the lids. Soon after the appearance of the ptosis he was troubled with double vision, a condition which has persisted. About five weeks before admission, owing to loss in the power of mastication, he was unable to chew solid food. In the past month he has had difficulty in speech; he has jumbled his words and states that he has "talked through his nose." A week before admission he completely lost his voice for a period of three days. For the same period his tongue felt thick; there has been a collection of mucus in his throat; he has had frequent cough and marked subjective dyspnea. There has been difficulty in swallowing, and fluids taken by the mouth have been repeatedly regurgitated through the nose. The patient has, however, been able to attend to his medical duties until three weeks ago, when great weakness of the upper and lower limbs compelled him to give up his work.

*Examination.* The striking feature on inspection was the patient's facial appearance. The drooping lids, the protruding, fixed eyes, the mask-like face, the open mouth and hanging jaw made a truly striking picture (see Fig. 1). He was weak, perspired profusely, and looked ill. He was unable to raise his head from the pillow, could scarcely raise his shoulders, and only with the greatest effort lift his arms from the bed. Dyspnea was so great that he was compelled to sit up in bed. Unable to expel the mucus

which collected in his throat, he had frequent, violent paroxysms of coughing. His voice had a distinctly nasal quality. He was clear mentally, but forgetful. He was emotional, and repeatedly burst into tears without assignable cause.

The exophthalmos was extreme. The other eye signs could not be tested on account of the complete bilateral ptosis and fixation of the globes. The thyroid gland was much enlarged, the right lobe more than the left, and was fairly soft and smooth. There was marked pulsation of the entire goitre, but no palpable thrill. On auscultation, a loud, systolic bruit could be heard over the entire gland; it was loudest over the superior thyroid vessels.



FIG. 1. - The striking facial appearance; the drooping lids, protruding fixed eyes, mask-like face, open mouth, and hanging jaw.

The pulse was regular and almost constantly about 120 per minute; the blood-pressure was 120 mm. Hg. The heart was not enlarged either to the right or left. A faint systolic bruit was heard over the apex; the sounds at the base were clear. There were no edemas. There was a well-marked tremor of the fingers. The hands and feet were sweating. Pigmentation was pronounced, particularly over the flexor and extensor surfaces of the extremities and about the trunk. Over the lower legs were several more or less circumscribed, brownish areas, and around the ankles there was quite a definite band of pigmentation. The skin of the abdomen was dark, especially about the waist line, where it was coffee-colored. There was some pigmentation of the skin of the forehead, deep

pigmentation about the genitalia, but none of the mucous membranes of the mouth.

Nausea, vomiting, and a rather persistent diarrhea, complained of during his illness, were absent during his stay in the hospital.

*Blood Examination.* Red cells, 5,600,000; hemoglobin, 100 per cent.; white cells, 9000; polymorphonuclears, 71 per cent.; eosinophiles, 1 per cent.; large mononuclears, 10 per cent.; small lymphocytes, 12 per cent.; large lymphocytes, 2 per cent.; transitionals, 2 per cent.

Examination of the lungs and abdomen was negative.

In the urine there was a trace of albumin in two of the four specimens examined and a well marked acetone reaction in three of them. Wassermann reaction was negative.

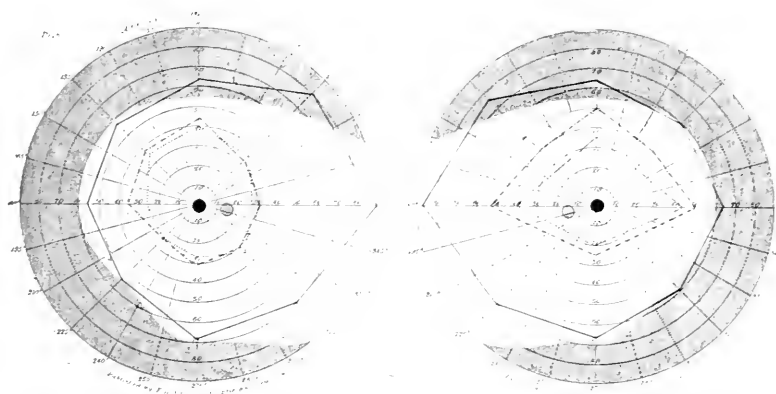


FIG. 2.—The eye fields, showing normal form fields, but contraction of the color fields, with interlacing of colors in right eye.

*Cerebral Nerves.* No disturbance in smell could be demonstrated. Taste also appeared to be fairly normal, although he mis-called salty and acid substances. There was complete bilateral ptosis of the eyelids. At rest the lids covered more than the upper half of either cornea. With the greatest effort the left upper lid could be raised slightly, but this movement seemed to be due rather to the elevation of the left eyebrow than to a true movement of the lid. The right upper lid could not be raised at all.

The greatly protruding eyes were practically fixed; there was no lateral, vertical, or rotary motion on either side. This total lack of movement of the globes persisted until the patient's death. Both eyes were directed forward in almost parallel lines. Double vision was constant, the upper image being the false one. Movements of the head from side to side had no influence on the position of the eyeballs, this test indicating an infranuclear rather than a supranuclear involvement. There was, therefore, a complete

ophthalmoplegia externa, a complete paralysis of the III, IV, and VI cerebral nerves. The pupils were usually but not constantly unequal in size, the left being larger than the right. They reacted promptly to light. The fundi were normal. The eye fields (see Fig. 2), showed normal form fields, but contraction of the color fields with interlacing of colors in the right eye.

The sensory fifth nerve appeared to be unaffected. There was no anesthesia of the conjunctiva and no sensory disturbance in the area of distribution of the trigeminal on either side of the face. The motor fifth, however, seemed markedly involved. The open mouth and hanging jaw were apparently due to the weakness of the muscles supplied by this nerve. At times the patient was unable to close the mouth; at other times he could, with a great effort, bring the teeth together. There was no evidence of contraction or atrophy of the masseters.

*Nerve VII.* Facial weakness was manifest on both sides, being more marked on the right than on the left. The face appeared placid and mask-like. The ordinary expressional movements were feebly executed. The patient could at times pucker his lips slightly and draw down the angle of the mouth; he was able to elevate the left eyebrow but not the right.

No disturbances in hearing could be demonstrated by the ordinary tests.

The voice, thick and indistinct, had decidedly a nasal quality; there was difficulty in articulation but no aphasia. The patient stated that his tongue felt stiff and awkward. Swallowing was difficult, and fluids taken by the mouth were in part regurgitated through the nose. There was a constant collection of mucus in the throat, which the patient seemed unable to expel. Cough was frequent and violent. Dyspnea was marked. The patient was able to protrude his tongue but slightly and the lingual movements were awkwardly performed. There was a marked tremor of the tongue. Examination of the palate and the pharynx was difficult. The palate appeared symmetrical. The pharyngeal muscles could be seen to move, but the examination was unsatisfactory. Sensation of the pharynx appeared to be normal. Examination of the larynx was unsatisfactory because of the patient's restlessness and the presence of mucus in the throat. Dr. Crowe stated the cords moved well on phonation.

The trapezius muscles were weak, the patient being hardly able to elevate his shoulders. Atrophy of these muscles was not demonstrable.

*Paracentral Region.* There were no gross sensory disturbances on either side of the body. There was, however, marked hyperesthesia of the skin. The patient complained whenever the skin was touched. This sensitiveness seemed especially pronounced over the abdomen and legs. The soles of the feet were extremely



sensitive, and the patient objected bitterly whenever plantar stimulation was attempted. There was no definite paralysis of the extremities, but a profound, general weakness. As has been stated, the patient was unable to support his head or to elevate his shoulders, he was barely able to raise his arms from the bed. The grip in either hand was practically *nil*. The muscular power in the legs was distinctly greater than in the arms. The muscular weakness seemed greater upon the right than upon the left side.

The reflexes were active at the knees and ankles. A suggestive ankle-clonus was obtained on one occasion. Plantar stimulation was unsatisfactory because of the extreme sensitiveness of the soles of the feet. The abdominal and cremasteric reflexes were normal. To Oppenheim's test there was a normal response.

*Summary of Neurological Findings.* Complete bilateral ptosis, complete ophthalmoplegia externa, paralysis or at least marked paresis of the motor fifth and of the seventh, bulbar paralysis, hyperesthesia of the skin, and profound muscular weakness.

*Symptoms Referable to Involvement of Ductless Glands Other Than the Thyroid.* The great muscular weakness, the pigmentation of the skin, and diarrhea suggested possible involvement of the *thymus* and *adrenal glands*. The pigmentation was most marked in places of pressure, that is, along the waist line, about the shoetops, and around the neck.

Symptoms suggestive of involvement of the *hypophysis* were also present. The body was quite fat, with a thick panniculus. The skin was soft, smooth, and feminine in appearance. The hips were rather broad. There was almost complete absence of axillary hair; the beard was less abundant than normal and there was absence of hair over the forearms and backs of the hands. The genitalia appeared to be normal. During the two months previous to admission there had been complete absence of all sexual desire.

Given the neurological findings which have been described, the question arose, Were we perhaps dealing with an organic lesion or lesions in the brain or with a myasthenia gravis? The picture presented by the patient corresponded closely with myasthenia gravis, which indeed has been observed associated with exophthalmic goitre. In that disease there may be ptosis, involvement of the eye muscles, the muscles of the face, of mastication, etc. All the voluntary muscles may become involved. Myasthenia gravis has been fatal in about 40 per cent. of the cases. Examination of the nervous system in this disease has revealed no abnormality. Of value in differential diagnosis is the myasthenic reaction of Jolly, the rapid exhaustion of the muscles by faradism. Our patient was tested for the myasthenic reaction on three successive days. Faradic stimulation sufficient to produce a good contraction of the muscles was employed. The muscles tested were usually the facial, the deltoid, and the quadriceps extensor of the leg. The stimuli were

applied at the rate of about 1 per second, and in all cases at least one hundred times, and sometimes for from two to five minutes. In none of the examinations could any fatigue of the muscles be demonstrated even after repeated stimuli. If this test is of value our patient was not a case of myasthenia gravis.

The patient remained in the hospital for six days. He refused operation. He was visited at his home, and in the ten days which elapsed between his first and second admissions there was no change in his condition. He finally consented to an operation, which was performed February 16, 1911, by Dr. Halsted. The condition of the patient was so serious that ligation of the superior thyroid arteries alone was done. Anesthetization was begun with the patient in a sitting position because of the orthopnea. His pulse rose to 170, and at one time to 180 during the operation, but at the end of the procedure his condition was satisfactory.

*Postoperative Course.* The patient was again carefully examined between eight and ten hours after operation. There was subjective improvement, the patient stating that he felt better than before the operation. Some slight movement of the globes was demonstrable, but this was not striking. His pulse was about 140. His temperature had risen to 101°. There had been some nausea following operation, but very little vomiting. He passed a fair night. During the following day (February 17) his pulse remained about the same, although at times it was slightly irregular. His temperature remained elevated. His blood-pressure, about 120, was unaffected. He eagerly took water, but the greater part of it was promptly expelled through the nose. There was a constant collection of mucus in the throat and frequent choking spells. About 8 P.M. of this day he complained greatly of shortness of breath, and became choked with mucus which he was unable to expel. His respirations suddenly ceased at 10 P.M., the heart continuing to beat. With the idea that there might be some obstruction to respiration a tracheotomy was promptly performed and artificial respiration undertaken. The heart continued to beat for perhaps five minutes during this procedure, and then ceased. Death, therefore, seemed to be due to an acute respiratory paralysis. Certainly, it was not a cardiac death, as is so often the case in exophthalmic goitre.

Most unfortunately an autopsy could not be obtained. A fragment of the thyroid gland, however, was removed, which showed the histological picture of Basedow's disease.

*LITERATURE.* The literature on cerebral nerve disturbances in exophthalmic goitre up to and including the year 1911 is considered with remarkable comprehensiveness by Sattler and Kappis. From these two authors chiefly and from the literature since 1911, I have obtained the following data as to the frequency of involvement of the various cerebral nerves.

1. Isolated palsies of the first or olfactory nerve have not been

reported in the literature, nor have isolated disturbances in taste. In combination with other cerebral nerve disturbances, loss of smell and taste has been observed in two cases of exophthalmic goitre (the cases of Warner and Bristow and of Ballet).

II. Isolated loss of vision has not been reported in exophthalmic goitre. Combined with other cerebral nerve disturbances the optic nerve has been affected in one case (Ballet), which showed diminished visual acuity on the left side with contraction of the visual field.

III. The third or oculomotor nerve has been most frequently affected and the majority of the cases reported have shown involvement of this nerve. Single muscles or all the muscles supplied by this nerve have been involved. Levator palsies and ptosis, either unilateral or bilateral, have been observed as isolated findings 9 times. Isolated rectus superior palsies have been reported 6 times and isolated rectus internus or convergence palsies 7 times. Of the latter, some observations seem questionable. Combined with other cranial-nerve disturbances the III nerve has been frequently affected. Isolated ophthalmoplegia externa, that is to say, palsy of the III, IV, and VI nerves, has been reported 6 times and an ophthalmoplegia externa combined with bulbar paralysis, as in our case, has been observed 5 times. The nerves supplying the internal muscles of the eye, *i. e.*, the pupils, have been affected in 5 instances.

IV. Isolated palsy of the fourth or trochlear nerve has been reported in one case; combined with other nerve lesions in 13 or 14 cases.

V. Isolated palsy of the motor fifth has not been observed; combined, this nerve has been affected 5 times, chiefly in cases of bulbar palsy. Involvement of the sensory fifth has not been reported except associated with a hemianesthesia.

VI. The VI nerve has, next to the III, been most frequently affected. Isolated palsy of this nerve has been observed 10 times. It has been frequently involved associated with the palsies of the III and IV nerves in ophthalmoplegia externa and in the cases with bulbar paralysis.

VII. Isolated palsies of the VII or facial nerve have occurred 5 times; combined with other cranial nerve disturbances 8 times.

VIII. Isolated involvement of the auditory nerve has not been reported. Combined with other disturbances loss of hearing has been noted in one instance.

IX. Isolated palsy of the glossopharyngeal nerve has been observed once. Combined, it has been involved in association with other nerves in the cases with bulbar paralysis.

X. The pneumogastric has not been affected alone. Vagus disturbances, however, have occurred in the cases with bulbar paralysis.

XI. The spinal accessory appears to be the only cranial to have escaped involvement in exophthalmic goitre. No true palsy of this nerve has been recorded either isolated or combined. Marked weakness of the sternomastoid and trapezius muscle has been observed in association with general muscular weakness, as in our case.

XII. Isolated palsy of the XII nerve has not been reported. Combined, this nerve has been involved in the cases with bulbar paralysis.

It may be seen from this brief summary that the nerves controlling the eye muscles are most frequently involved in exophthalmic goitre. Kappis was able to collect over 40 cases in which the eye muscles alone were affected. Isolated palsies may occur, but combinations of various kinds are most commonly seen. A pure ophthalmoplegia externa, as previously stated, has been observed in 6 cases.

With the exception of palsies of the facial, 5 cases of which have been reported, isolated palsies of the remaining cerebral nerves are extremely rare. Combined palsies of these nerves, as recited, are not uncommon, and the most varied clinical pictures occur.

The cases with bulbar paralysis form a most interesting group, and deserve perhaps more than passing mention. They have all been severe cases of exophthalmic goitre, and in most instances the disease has run a rapid course. In one instance the patient had had a goitre for many years, on which Basedow had become engrafted.

The duration of the disease has varied from a few days to five or six months before the onset of bulbar symptoms. Death has invariably followed the appearance of these symptoms, and in the majority of instances within a short time. One case died one day, another three days, and another eight days after the onset of bulbar symptoms, while others have lived from several weeks to three months thereafter. We may, therefore, divide the cases into those with acute (the majority) and those with chronic bulbar palsy. Our case is of the latter group. While there has been considerable variety of combination in the nerve palsies, the bulbar symptoms have been remarkably uniform in all the cases.

It is difficult, from the reports of cases in the literature, to differentiate the cases of bulbar paralysis due to organic lesion from those of myasthenia gravis with bulbar symptoms; and it is possible that some of the 12 cases assigned to true bulbar palsy do not correctly belong in that group. The cases were all reported between 1886 and 1901, and 8 of them before 1900. The myasthenic reaction was tested, apparently, in very few instances, if at all. We have, therefore, to base our opinion largely on the clinical course of the paralysis. Autopsy findings are suggestive but not altogether convincing. In 6 of the 12 cases an autopsy was not done, or no mention is made of it. In 1 of the remaining 6 cases a definite

lesion was found in the nuclei of the affected nerves, described either as an area of softening or of fresh encephalitis. In the remaining 2 cases it is stated that gross lesions of the brain were not present; but serial sections for microscopic examination were not made, and therefore these negative findings are inconclusive: 2 of the 12 cases certainly suggest a myasthenia gravis chiefly because of the variability in the palsies. In neither of these 2 cases was an autopsy obtained.

**ETIOLOGY OF NERVE PALSIES IN EXOPHTHALMIC GOITRE.** As regards the etiology of nerve palsies in exophthalmic goitre, it may be said that no very definite knowledge is at hand. It is assumed that the disturbances in the cerebral nerves are of a toxic nature, the toxins being responsible for the lesions in the nuclei of the cerebral nerves. Clinically, there is some evidence for this assumption, for palsies occur, as a rule, after the disease is well established, and never, so far as is known, in cases of cured exophthalmic goitre. Cases are known, however, though they are very rare, in which palsies appeared shortly before the outspoken symptoms of Basedow's disease, while in a few instances the palsies and the usual symptoms of exophthalmic goitre have appeared simultaneously.

**PATHOLOGY.** In 4 of the 6 cases with bulbar paralysis in which autopsies were obtained, definite lesions were present in the medulla associated with extensive degeneration of fiber tracts. The 2 cases with negative findings are not conclusive, for a careful examination of the brain was not made. It has been in the cases with bulbar paralysis that the most positive pathological findings have been obtained, for they have all been severe cases of exophthalmic goitre which have quickly terminated fatally. In the great majority, the palsies have affected chiefly the eye muscles and apparently have not influenced greatly the course of the disease. These cases have gone from observation and the end result has not been known. In brief, it may be said that comparatively few pathological lesions in the brain have been recorded in the cases of exophthalmic goitre with nerve palsies. This may perhaps be explained (1) by the fact that they rarely have been looked for, (2) because the majority of the patients have not died while under observation, and (3) because serial sections of the brain have not been made—a necessity for the demonstration of a small lesion.

**THE CLINICAL COURSE OF THE CEREBRAL NERVE PALSIES.** The palsies may appear at any stage of the disease. In most cases they manifest themselves months or even years after the onset of the disease; in one case it was not until six years after the first symptoms of exophthalmic goitre that the palsies were noted. They may, however, begin acutely, simultaneously with or soon after the other symptoms. In a few instances the palsies have been reported as the first symptom of Basedow's disease. In most cases they

have entered the clinical picture almost unobserved, the disease not having become noticeably more serious with their occurrence. But the palsies may, as stated above, begin acutely and spread rapidly. In some of the cases reported it has developed over night, and synchronous with the rapidly spreading palsies there has been a marked increase in the severity of the disease.

In cases in which several nerves were involved there seems to have been no uniformity as to the order in which the paralysis appeared. Frequently they have occurred almost simultaneously, but they may follow one another at irregular intervals. The period between the onset of the first palsy and that of the last has not been great—less than a year in the vast majority of cases, but two years in a patient of Kappis. The complete paralyses have usually persisted unchanged. In no case has the palsy been benefited by operation, although marked improvement in other symptoms has been noted. There are apparently 2 cases, however, in which palsies of short duration have disappeared on improvement of the other symptoms, and 3 cases in which there was a partial recovery of the palsies.

What has been said thus far regarding the clinical course of these palsies does not hold for the cases with bulbar paralysis. These cases have, without exception, been highly toxic, the palsies have been rapidly progressive, and a fatal termination has quickly followed.

**DIFFERENTIAL DIAGNOSIS.** I shall merely mention some of the conditions in exophthalmic goitre which may simulate the true palsies. As has been said, myasthenia gravis undoubtedly may be associated with this disease. Sattler gives abstracts of 6 cases in which a positive myasthenic reaction was obtained. In addition to the myasthenic reaction a fairly characteristic finding in the cases of myasthenia is the variation from day to day in the palsies. Brain tumor has been noted in one case of exophthalmic goitre with nerve palsies. Cerebral hemorrhage, multiple neuritis, and multiple sclerosis have all been observed associated with exophthalmic goitre, and it is possible that these complications might give rise to some difficulty in diagnosis.

**PROGNOSIS.** A few additional words may be said as to the prognosis in the cases of Basedow with nerve palsies. Slight palsies, as those of the eye muscles, such as occur in the majority of the cases do not necessarily make the prognosis more grave. The paralyses themselves do not lead to death; the prognosis depends, as I have said, upon the severity of the Basedow. If the paralyses develop slowly, or acutely if merely to a slight extent, they have a serious significance *per se* only when they involve important nerves such as the vagus, which occurred in one case of Kappis. In the cases with very acutely developing and at the same time extensive paralyses the development of a bulbar paralysis is to be feared.

The occurrence of a bulbar paralysis makes the prognosis very grave, for, as has been previously stated, death has invariably followed.

TREATMENT. Only 4 cases have been operated upon. In 2 cases reported by Kappis the operation had no effect on the eye palsies, although the cardinal and other symptoms of exophthalmic goitre were greatly improved. So far as I am aware the case which I am reporting is the first of the grave ones (with bulbar paralysis) to be operated upon. Kappis reported a third case, one with difficulty in swallowing, which was believed to be due to paralysis of the glossopharyngeus and vagus. The patient died four hours after a lobectomy.

The presence of nerve palsies, excluding possibly the cases with bulbar paralysis, does not contra-indicate surgical intervention. Indeed, it would seem advisable to operate promptly in the hope not only of arresting the progress of the palsy but also of curing the disease.

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### THE METABOLISM AND TREATMENT OF RHEUMATOID ARTHRITIS. THIRD PAPER.<sup>1</sup>

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IN two previous communications<sup>2</sup> the writer has presented a series of cases of rheumatoid arthritis, 18 in all, in which certain laboratory findings and clinical observations were made the basis

<sup>1</sup> Reported before the American Society for the Advancement of Clinical Investigation, Washington, D. C., May 10, 1915.

<sup>2</sup> The Metabolism and Successful Treatment of Chronic Joint Disease; A Preliminary Report, AMER. JOUR. MED. SCI., October, 1912, No. 4, cxliv, 474; and The Metabolism, Prevention, and Successful Treatment of Rheumatoid Arthritis; Second Contribution, *ibid.*, December, 1913, No. 6, cxlvi, 895; January, 1914, No. 1, cxlvii, 111; February, No. 2, p. 265; March, No. 3, p. 423.

of a method of treatment. The results of this were sufficiently encouraging to justify and require a more extended study, with the idea of determining not only the proportion and kinds of cases in which benefit could be expected, but also, if possible, the *modus operandi* of the factors concerned.

The methods in question consist essentially in a curtailment of diet, particularly the carbohydrates and proteins, to a point of tolerance which varies with the individual.

An additional series of cases of rheumatoid arthritis, 19 in number, has accordingly been treated and studied. It is the purpose of this article, therefore, (1) to review the end-results of the first series, where this is possible, some of them dating back five years; (2) to present the results of treatment of the second series of cases, together with some analysis of the failures and successes; (3) to present the results of certain feeding experiments in which the effort was made to determine the specific action, if any, of some foods; and (4) to present the results of laboratory observations, especially upon the hydrogen ion concentration of the urine and the carbon dioxide tension of the alveolar air during the active stages of the disease and during convalescence or recovery therefrom.

END-RESULTS OF THE FIRST SERIES. The first series consisted of 18 cases, and a review of them at the present writing brings out several interesting points. No attempt will be made to go into the details of the cases, as these have already been fully given.

Case I was first seen in January, 1911, and remains well, nearly five years afterward.

Cases II, IV, IX, XIII, XVI, and XVII have disappeared from observation.

Cases III and VIII were temperamentally unable, except under close observation, to adhere to any careful régime involving self-denial, and after becoming practically free from active symptoms, deliberately ate what they chose and relapsed.

Cases V and VI are entirely well and leading active lives.

Case VII has run a course of much interest. After making a symptomatic recovery, she slowly lost ground, and in July, 1914, a strict diet modified only slightly an active arthritis. In August she developed acute intestinal obstruction, was operated upon by Dr. John Kennedy, of Philadelphia, and a stenotic band was relieved, after which her arthritis was greatly improved. She felt so well that she ate much more generously, adhering only slightly to the lines of her earlier diet. Her arthritis grew slowly worse, and when last seen, March, 1915, she had definite symptoms, though less than at some previous periods.

The beneficial influence of diet in this case when first treated, the violent exacerbation just preceding acute intestinal obstruction, the relief of symptoms during a long period following the operation, and the gradual increase of the arthritis at first influenced



by a diet and then increasingly less so form a most suggestive sequence of events.

Case X remains well, on duty as a hospital attendant.

Case XI, who was bed-ridden, is free from active arthritis, gets dressed, and walks around one floor of her home. Her chief limitation comes from the ankylosis of her knees in extension, present when first seen. It is of interest to note that there has been present throughout an active leucorrhea which was not properly treated because of the inability to abduct the patient's thighs. This still persists, though the thighs can now be abducted. Her original and subsequently maintained improvement in the face of an obvious source of possible infection is of much interest.

Case XII is reported as active and walking without crutches, and Case XIV is on active duty as a nurse.

Case XV is in buoyant health, and has acquired a considerably increased tolerance for food.

The degree to which patients in this series have differed in their caloric necessities has been noteworthy. Several of them have maintained constant weights upon fewer calories than are generally regarded as practicable in ambulatory cases, as previously noted.

NEW SERIES. Space will not permit of giving more than a bare outline of the cases and treatment in this series, together with certain limitations to treatment, except where some particular point necessitates it. In the previous series the full details of each case, together with frequent notes showing the changes of diet and progress, make a repetition of these data in connection with the present cases unnecessary. It should be stated that every case but one was Roentgen-rayed by Dr. W. S. Newcomet, director of the Roentgen-ray department of the Presbyterian hospital, and the clinical diagnosis of arthritis was always thus corroborated. Nearly all of the chronic cases had been through more or less treatment, and some had experienced a great variety.

CASE XIX.—Mrs. L., aged sixty-four years, referred by the courtesy of Dr. Walter L. Mendelson, of New York City, was admitted March 28, and discharged June 29, 1914. She presented exophthalmos, enlargement of the thyroid, some tachycardia dating back twenty-five years, an enlarged heart and murmurs. The arthritis was of ten years' duration, affecting the knees, shoulders, and hands. For ten days the patient was watched upon an unrestricted house diet and lost three pounds in weight, averaging 2346 calories per diem, and on April 6 she was given a mixed diet of 1385 calories. By a mixed diet is meant one consisting roughly of one or two eggs, from two to six 30 gm. slices of bread, about 50 gms. of chicken, 15 to 30 gms. of butter, and about 15 gms. of sugar plus green vegetables, according to the desired total. In three days there was some improvement, and on the eleventh day there was no pain in any finger or in the wrist on pressure.

June 17, 1915. Has been doing progressively well for two months. For a month the effort has been made to increase diet, body fat, and weight. Today she feels for the first time some tenderness in the last joint of right ring finger.

The patient left the hospital June 29, with greatly increased bodily activity and hands free except as per last note. Weight, 123 pounds; loss, 16 pounds. She spent the summer at a hotel and followed the diet as well as she could, but grew restive under it. She was seen with Dr. Mendelson in November, 1914. The arthritis of the right ring finger was worse and one other small joint was involved. Her bodily activity, knees, and shoulders were much improved, especially the former two.

Retrospect of this case reveals that the hyperthyroidism was a complicating factor and added to the difficulties of treatment, in that the patient ran an increased pulse-rate throughout and tended easily to lose weight. The long stay in the hospital helped her tremor but made her restive. Her diet was increased too soon, and she admitted that after leaving the hospital she had taken some liberties with it. The entirely favorable application of diet to her arthritis was beyond question, however. The result from her stand-point was an improvement, modified and limited by the complicating hyperthyroidism and by the personal element which led to a curtailment of treatment short of the theoretical ideal.

CASE XX.—Mr. F., aged about fifty-five years, was referred by the courtesy of Dr. Milton J. Lichty, Cleveland, Ohio. Admitted April 9, 1914, discharged July 6, 1914. An arthritis of four and a half years' standing involved practically all joints, and he was confined to a wheel-chair. A probationary house diet showed 3500 to 4000 calories. After several changes the new mixed diet was maintained at 1485 calories. Improvement in the hands began in six days. No changes occurred in the ankylosed joints, but when the patient left the hospital on July 6, 1914, his hands had greatly changed their appearance and he had less pain generally. The loss of weight in three months was twenty-four pounds. This patient was beyond everything but the arrest of the disease in its then stage, but there cannot be any doubt that the causative arthritis was emphatically modified, and in the smaller joints had largely subsided when he left.

CASE XXI.—Mrs. H., aged sixty-three years, was referred by the courtesy of Dr. Hobart A. Hare. She presented an arthritis of four years' duration, involving the knees, shoulders, and hands. She was obese, with myocarditis and loud murmurs. A probationary house diet averaged 2024 calories. She was given a mixed diet of 1271 calories and after six days showed a beginning subsidence of inflammation in the hands. She developed cardiac irregularity and beginning loss of compensation after two weeks of restricted diet, requiring complete rest in bed and stimulation. This diet

was insufficient to accomplish permanent results and evidently a further reduction was necessary. In view of the heart condition, however, such a step was regarded as dangerous. The patient adhered faithfully to the above diet for three months without any additional improvement in the hope that, though insufficient to arrest the causative arthritis, something might be accomplished. The end-result to her, however, was absolutely *nil*. This case is of value as illustrating the fact that in face of a beginning and distinct response to treatment, as evidenced in the hands, limitations from another source may preclude further efforts. It is important on many counts, as illustrated above, to keep the caloric total as high as possible, from which it follows that in many cases several or more diets have been required before the proper reduction was obtained.

CASE XXII.—Mr. P., aged thirty-one years, was referred by the courtesy of Dr. Penn G. Skillern. An arthritis of nine months' duration, immediately following a severe infection of forearm, incapacitated him for work by involvement of hands, knees, and shoulders chiefly. There was no apparent focus of infection anywhere. The patient was a large eater, and began to recover upon a mixed diet of 2500 calories, which were reduced in ten days to about 2000. Progress was steady from the start, and he went home well. Admitted March 3, 1914. Discharged May 2, 1914. Last heard from and well October 15, 1915. The loss of weight in hospital was from 134 to 127 pounds.

CASE XXIII.—George W., aged forty-five years, ward case, was admitted June 26, 1913. An arthritis of eight months' duration, involving knees, heels, shoulders, and hands, incapacitated him. His condition was febrile and somewhat suggestive of acute inflammatory rheumatism superimposed on the chronic form. He was given a very low mixed diet of 629 calories for ten days. Undoubted subsidence of the acute symptoms followed. The calories were increased to 1072. The case was not followed beyond July 12, 1913, but the evidence was definitely favorable until then.

CASE XXIV.—Mrs. McC., aged fifty-four years, admitted May 25, 1914, discharged August 20, 1914, presented a chronic arthritis of uncertain duration. There were also redness, tenderness, and effusion in knees, ankles, hands, and wrists. Practically every joint was involved, and the symptoms pointed to an acute and severe inflammatory process on top of the chronic form. She was given five glasses of milk in twenty-four hours, increased by eggs chiefly, in course of one week to 1011 calories. Her joints responded from the start, becoming in six days practically painless. Within two days after admission she developed signs of pneumonia, and had a delayed recovery therefrom. The calories were later increased to 1950 to meet the convalescent demands. In January, 1915, her general condition was excellent and the joints were in tolerably

good shape. The social condition of the patient precluded intelligent coöperation.

CASE XXV.—Mrs. R., aged thirty-three years. Was admitted May 22, 1914, discharged July 10, 1914, and had an incapacitating arthritis of three months' duration involving hands, elbows, and knees. Bony deformity of the fingers was present. A probationary house diet averaged 1916 calories. On a mixed diet of 1314 calories she improved at once and steadily. She left the hospital almost free from all symptoms, and has remained entirely well since.

CASE XXVI.—Mrs. S., aged forty-five years, was admitted May 13, 1914, and discharged May 22, 1914. An arthritis of three years' duration involved hands, wrists, elbows, shoulders, knees, and ankles. On a probationary house diet of 1734 calories she began to improve at once and left the hospital against advice when the subjective symptoms had subsided. This case is reported to illustrate the occasional improvement which follows upon the restricted régime of a hospital diet. Comment on this will be made later. Had she stayed a permanent limit of intake would have been assigned her, in the attempt to insure against relapse.

CASE XXVII.—Mrs. C., aged thirty-five years, referred by the courtesy of Dr. A. A. Eshner, was admitted April 27, 1914, and left May 24, 1914. An arthritis of three years' duration involved both hands, wrists, elbows, shoulders, knees, ankles, and feet. A probationary house diet averaged 1933 calories. She improved on 1179 calories of mixed diet, but after ten days became dissatisfied with restrictions and left against advice.

CASE XXVIII.—Mrs. F., aged thirty-nine years, was admitted February 8, 1915, and left February 27, 1915. An arthritis of two years' duration involved spine, jaws, shoulders, elbows, hands, and knees. Four months pregnant. Many fibrous nodules presented along ulnæ, tibiæ, and around patellæ. She showed some improvement on probationary house diet of 1494 calories, and was given 1396 calories of a fixed diet to insure constancy of intake. Rapid and unmistakable progress followed. She became dissatisfied with restriction of diet, and left against advice. The fibrous nodules had markedly subsided.

CASE XXIX.—Mrs. L., aged about forty-two years, wife of a physician, was referred by the courtesy of Dr. D. J. McCarthy. She was admitted April 19, 1915, and discharged July 5, 1915. An arthritis of nine years' duration involved the shoulders, elbows, wrists, hands, and feet. There were fibroid nodules on both Achilles tendons. A probationary house diet yielded 1850 calories, and she was given a mixed diet of 1191 calories, reduced in two weeks to 1028. Progress was slow but sure. The fibrous nodules and three-quarters of the painful sites were practically gone when she left the hospital. She was instructed to follow her diet all summer

and report in the fall. The loss of weight was from 116 to 105 pounds.

CASE XXX.—Mrs. W., aged about forty-nine years, wife of a physician, was referred by the courtesy of Dr. B. W. Sherwood, of Syracuse, N. Y. Admitted April 20, 1915, discharged June 12, 1915. An arthritis of two and a half years' constant duration, dating back irregularly thirteen years, involved the shoulders, elbows, and hands. This case was of much interest, and was a complete failure. The probationary house diet yielded 2048 calories. New diets were tried of 1294, 1159 and for a short time 674 calories, without clear improvement. An abdominal *x*-ray was not taken, as customarily on admission, as patient had had this done and the results were reported negative. Upon failure of treatment an *x*-ray was taken and showed a high degree of visceral stasis, partial collapse of the large bowel, evidence from the bismuth of obstruction in or near the ileum, chronic appendicitis, and possibly duodenal ulcer. The reason for failure cannot be advanced unless it be dependent upon these findings, especially the first two. In discussing the failure with Dr. Sherwood, before the *x*-rays were taken, the writer cited Case VII (*q. v.*), as supplying a possible explanation in the obstructive factors there operative. The patient's condition did not suggest, *a priori*, any difficulty of treatment.

CASE XXXI.—Mrs. W., aged about forty years, was referred by the courtesy of Dr. John H. Girvin. A multiple arthritis had for some years involved shoulders, elbows, knees, and hands. Some improvement followed a probationary house diet of 1544 calories. The patient had bad tonsils, and these were removed. It is interesting to note that upon the two days immediately following the operation the patient felt great relief in her joints everywhere, during which time she was nearly without food. As the food was increased the pain and disability returned. The patient then went home to ascertain the end-result of the tonsillectomy, but of her own accord attempted to follow a diet of 1433 calories which she had been given for a few days at the hospital prior to the operation. At this point she disappeared from observation, but was reported later as doing very badly. The points to be noted in this case are the prompt and marked relief coincident with postoperative starvation, ceasing as ingestion of food increased; and the difficulty to be met when patients attempt dietary control by themselves before they are thoroughly accustomed by experience accurately to prepare and follow a diet. Earlier observations on the postoperative relief above recorded helped the writer to formulate the hypothesis upon which this study was started.

CASE XXXII.—Mrs. W., aged about sixty-two years, was referred by the courtesy of Dr. Agnes Viotor, of Boston. Admitted March 9, 1915, discharged June 9, 1915. An arthritis of thirty

years' standing involved nearly every joint in the body except spine and jaws. Myocarditis and mitral regurgitation were present. A probationary house diet yielded 1945 calories. She was placed on a mixed diet of 1080 calories, and improvement began at once, especially in the hands. After one month the case "hung fire." The calories were changed to 1283, of which 753 came from fat. The joints improved further, but her heart-rate increased to 108 and the patient became weak. Her diet was therefore increased eventually to 1700 calories. Her general condition grew stronger, the pulse fell to 85, the pains returned somewhat, especially in knees, but her hands retained their objective and subjective improvement (loss of weight from 161 to 145 pounds). She was instructed to follow this compromise diet all summer. This case showed unquestionable and satisfactory response to diet, but her heart was unequal to carrying her through in the way desired.

CASE XXXIII.—Dr. X., aged thirty-eight years, noticed in early January, 1915, a slight tenderness of the middle joints of some of the fingers of both hands. Toward the end of February there was added to this an ache involving also the lumbar spine. An x-ray, taken and interpreted by Dr. Henry Pancoast, director of the x-ray department of the University of Pennsylvania Hospital, showed inflammatory fog around the affected joints together with rarefaction and overgrowths along the shafts of the bones, an interpretation shared by Dr. Newcomet. Being familiar with some of the writer's cases the patient attempted a diet, and in ten days lost six pounds. He had always been a large eater, particularly of starches and sugars. When seen by the writer he was given a mixed diet of about 1200 calories, and by eight or ten days subjective improvement was established. During an attack of influenza, which then began, he lost more weight, but after about six weeks of adherence to his diet he was entirely free from symptoms, and during August took part in a military encampment, by this time eating much more generously. The diet was carefully carried out in this instance, and the patient himself weighed the ingredients on scales. The loss of weight was about ten pounds in all, from 173 to 163.

FEEDING EXPERIMENTS. The following cases will be detailed at greater length, because they were the subjects of experiments in feeding which developed several points of interest. These experiments were conducted with the full understanding of the patients, who appreciated the possible importance of their coöperative efforts.

CASE XXXIV. —Mrs. S., aged thirty-six years, referred by the courtesy of Dr. Frank Dickson, was admitted November 9, 1914, and discharged February 23, 1915. An arthritis of over seven years' duration, involved the jaws, shoulders, elbows, wrists, ankle, and knees; the hands slightly; the right knee was resected seven years

before. A probationary house diet yielded 1892 calories. On 1072 calories of mixed diet, she improved slowly but steadily, and on January 9, being up and out daily and feeling well, she was given the diet presently to be described.

It should be here stated that for some time the writer had been following the hydrogen ion concentration in the urine of joint cases at various stages of their progress, but no definite conclusions could be reached. The variations of diet in the same and different cases seemed apparently to mask any reaction or fluctuations due to the disease itself, and it was not until the appearance of Blatherwick's "Studies"<sup>3</sup> on the nature of the ash in various foods and its influence upon urinary acidity that these relations became clear and a standard diet could be applied. Accordingly in the following cases one of the diets there described has been utilized as a basis for the study of the urinary acidity of joint cases in health or disease, and also when the influence of certain foods was tested. These standard diets were made up equivalent in caloric value to the mixed diets under consideration, and were chosen without other regard to therapy. The patient was therefore given graham crackers, 75 gms., butter, 36 gms., milk, 720 c.c. per diem = 1009 calories. This was continued for ten days to allow her condition under it to be watched and the urinary acidity to be followed while she was free from symptoms. The basis upon which all the cases in these series have been treated is, in part, that the carbohydrates form at least one of the factors productive of joint disease, and favorable results have followed their curtailment. Other evidence pointed the same way, but the "experimentum crucis" had not been made of inducing the symptoms of the disease by means of pure carbohydrate in a patient previously rendered free from them—a reinroduction of the disease, in short.

On the afternoon of January 19, therefore, and twice daily thereafter, the patient was given 62 gms. of "candy" made from cane-sugar, water, a little oil of peppermint to flavor it, and one teaspoonful of vinegar to 528 gms. of sugar. This gave 66 gms. of sugar at each feeding, or 264 calories twice a day, a total ingestion of 528 calories in addition to her regular diet. The total for twenty-four hours was therefore 1089 plus 528, or 1617 calories, an amount somewhat less than the house diet on admission, but considerably greater than that upon which she had improved. It is to be remembered that at this point she was practically free from symptoms, up all day and taking exercise on the porch. The abbreviated notes of her progress follow:

January 22. One joint of left hand shows a slight sensitiveness not present for at least a month.

January 23. Pain increased and present in shoulders and wrist.

<sup>3</sup> The Specific Role of Foods in Relation to the Composition of the Urine, N. R. Blatherwick, Archives Int. Med., September, 1914, xiv, 409-450.

January 24. Hand slightly better. Left shoulder worse. Painful red swelling with effusion just above left elbow. Not sore for six weeks.

January 25. Thumb better but still sore. Elbow and shoulders as before. Jaw on the left painful. Patient is very uncomfortable.

January 26. No candy given today. Jaws worse, both sides equally. Shoulders better. Thumb and knuckles about the same.

January 26. Better as a whole. Jaws, shoulders, and thumb ache less. One joint of left hand has ceased to hurt. Pressure over seventh cervical vertebra elicits soreness and suprascapular muscles on left ache. Undoubted improvement.

January 28. Muscles of back and seventh cervical vertebra are the chief sites of pain. Today patient returns to the mixed diet of 1089 calories, taken before the graham-cracker diet, as the latter has become very monotonous.

January 29. About the same.

January 30 and 31. Better.

February 2. Improvement continues. Muscles of back and neck and the left elbow show some residual soreness. Progress from this date was entirely satisfactory and continued so. Last seen December, 1915, when improvement was maintained. Loss of weight in hospital from 158 to 143 pounds. Comment on this experiment will be made later.

CASE XXXV.—James N., aged forty-four years, referred by the courtesy of Dr. T. T. Thomas, was admitted November 12, 1914, and discharged March 23, 1915. An arthritis of four years' duration, involving shoulders, elbows, wrists, hands, hips, knees, and ankles, incapacitated him. He made noticeable progress on a house diet of 2170 calories, and after a variety of diets of lower caloric value from 1512 to 1829, made steady progress, subject to occasional exacerbations of an acute nature, generally with some effusion. During three months these became less severe and he recovered from them more rapidly, being increasingly free from chronic symptoms in the interim. It was obviously necessary to wait until these exacerbations had become negligible and until observation of the case over a long period of convalescence had shown its true course before a feeding experiment comparable to the last could be attempted. After the patient had been given six or seven different diets, had been watched through six decreasing exacerbations of his chronic arthritis, and was free from pain anywhere in his body, it was thought, on February 16 1915, that a repetition of the carbohydrate feeding would be justified and that any clear response could be ascribed to it. He was accordingly put on 1827 calories, consisting of graham crackers, 100 gms., butter 10 gms., one cup of weak tea with 7 gms. sugar, and one apple of 150 gms. three times a day. For six days he had had practically the same thing, except that 360 of the calories



had been supplied by three glasses of milk per diem; but it was thought advisable to remove, as far as possible, all protein from the diet so that any disturbance referable to the food intake must be due to some other factor in it. Prior to this he had been taking 1512 calories of a mixed diet. A difficulty to be here considered, which had been operative in certain earlier indefinite experiments, was that the patient's total caloric tolerance seemed to be pretty high, as evidenced by the house diet of 2170 calories, on which he showed improvement. This must be exceeded considerably by the sugar calories to have any effect, and such an addition might be physically and psychically difficult of accomplishment. There is a very definite limit to the amount of pure carbohydrate one can willingly take for any length of time. However, beginning with February 16, he was given twice daily 138 and then 150 gms. of candy, made as described in the first case, but without any vinegar. This was equivalent to 150 gms. of cane-sugar, or 600 calories. The patient professed at first to like this and ate it readily, but later did so with great difficulty. The notes of his progress follow.

February 17. Says he feels a little bit stiff in both shoulders, knees, and feet.

February 18. Feels somewhat "tired." Shoulders and knees slightly stiff, but very little so.

February 19. About 7 P.M. yesterday began to feel pain and stiffness in left shoulders, after which pain developed in feet and other joints. Today he has pain on active or passive motion or on pressure at left shoulder, both wrists, between the first and second metacarpophalangeal articulations of left hand, at right thumb (slightly), at second metacarpophalangeal joint of left hand (which hand cannot be closed as usual), at midjoint of middle finger of left hand, and near internal malleoli of both ankles. He cannot rise on his toes as well as usual and does so with considerable pain. Is quite wretched and could not be kept on this diet any longer. There is possibly some fluid in midphalangeal joint of midfinger of left hand. Same point on right hand is slightly sensitive to pressure. "Jumps" visibly if a sore point is touched. Ate no supper last night or breakfast or dinner today. Candy to be stopped. Has had none since 4 P.M. yesterday.

February 20. Much better. Points still showing tenderness are wrists and hands, which are much improved. Took one meal of graham-cracker diet yesterday and all three today.

February 21. A trace of tenderness in one joint only.

February 22. Feels very well.

February 23. Diet changed to a mixed one of 1512 calories.

This patient's further progress was uneventful, and he went home feeling entirely well on March 23, except that on March 3, under some rather forced mixed feeding to make up for the loss of

weight sustained during this last attack, patient developed some toothache, a red throat, some joint discomfort, and fever, the latter up to  $100\frac{3}{4}^{\circ}$ . He had been losing weight or remaining stationary, but as the result of this feeding had gained five pounds in all. His diet was again sharply cut and he improved at once. The patient was still well six weeks after leaving the hospital, and though he deliberately departed from his diet after July, and gained 20 pounds, he was in very fair shape in November, 1915.

The results in this case seemed pretty clear. There could be no question of his original illness; of his marked convalescence; of the exacerbation under the sugar feeding; of his prompt convalescence when the sugar was removed (hastened, possibly, by his refusal of all food for nearly twenty-four hours), or of the excellence of his condition when he left the hospital. The only doubt that can enter is, whether there could have occurred a severe exacerbation coincident with the experiment, such as those noted early in the course of treatment and referred to above. The diminishing nature and frequency of these attacks, their practical cessation under strict diet and their somewhat different character make this unlikely.

CASE XXXVI.—Miss C., aged thirty-five years, referred by the courtesy of Dr. E. H. Goodman, came under observation February 1, 1915, and was discharged July 7, 1915. An arthritis of four years' intermittent duration involved the jaws, shoulders, elbows, hands, knees, and ankles. The patient had wide-spread and severe psoriasis, involving nearly every part of the body. Treatment of this case developed several points of interest. Her previous treatment had included vaccines and radium water. She began to improve on a house diet of 1718 calories. On February 18 she was given a diet of 75 gms. of graham crackers, 1 apple, 5 gms. butter, and 9 gms. sugar at each meal, yielding 1410 calories a day, with the idea of maintaining the joint improvement and at the same time helping the psoriasis along lines indicated by the interesting work of Schamberg, Ringer et al.<sup>4</sup>

These authors have shown that there is in psoriasis a strong tendency toward the retention of nitrogen and that a curtailment of the nitrogen intake to a minimum may be followed by great improvement or cure. By March 16, 1915, it was evident that the psoriasis had improved about 75 per cent., but that the joints, after having made substantial progress and changed their shape, were "hanging fire." She was then put upon a mixed diet of 1002 calories, on the possibility that the carbohydrate intake was too high. After eight days she had lost 9 pounds *in toto* from the start, her weight being 110 pounds. It was thought that a still more restricted diet was indicated, but that preparatory to putting

<sup>4</sup> Research Studies on Psoriasis, Schamberg, Kolmer, Ringer, and Raiziss, Jour. Cutan. Dis., October and November, 1913.

her upon it an effort should be made to increase her weight and strength. This was a mistake, but she was put back, March 24, 1915, on a fuller diet, very high in carbohydrates but low in nitrogen, and consisting of bread, potatoes, rice, etc. The hope was that the psoriasis could be held in abeyance while her weight was increased even at the expense of her joints, but she relapsed so promptly and severely that on March 30, 1915, the psoriasis was everywhere violent and the arthritis as bad as it had ever been, or worse. It was felt that radical measures alone would do her any good, and she was put upon a graham-cracker diet as above of 846 calories. The joints responded at once, objectively as well as subjectively, and by April 11, 483 calories of fat had been added in the shape of olive oil and butter, with the idea of increasing her weight, which had gone down to 103 pounds, and also of testing out her tolerance for fat as compared with carbohydrate. Her weight reached 101 and then began to climb. The psoriasis showed no real improvement this time on the low nitrogen diet, though the nitrogen intake was lower than before, and at her request she was given, by Dr. F. C. Knowles, on April 13, an ointment containing liquor carbonis detergens and salicylic acid, after which the psoriasis improved. Her further progress was steady, and by April 21 she was taking 2054 calories, of which only 860 came from the graham crackers and apples. On June 14, 1915, the woman was practically well of both her psoriasis and joint disease, save for a very trifling sensitiveness on lateral pressure over the middle knuckle of the right midfinger. The ointment had been stopped on June 2. She had often previously been on full doses of the salicylates without benefit, and was two weeks convalescent as to her joints when the ointment was started.

It was thought that this would be a good case in which to try the effect of high carbohydrate feeding, as in the last 2 cases, so on June 20, all fat was substituted by pure carbohydrate in the form of peppermint candy. She was getting a total of 2053 calories, of which 1207 came from fat and whisky. This was substituted by 300 gms. sugar, equivalent to 1200 calories, but as no injury was apparent on the 24, she got a further addition of 40 gms. corn-starch and 35 gms. sugar, equivalent to 300 calories, making the total 2353. On June 26 she was still well, however, except for a bad headache, and could not force down her food, so the experiment was stopped. She was put back on the high fat diet, substituting saltines for graham crackers, and left for home July 6, apparently perfectly well. Before the forced carbohydrate feeding her weight had come up under the fat to 105, and when she left it was 109 pounds. It is hard to escape the view that the psoriasis was a complicating factor in this case. The caloric reduction was almost the lowest the writer had ever reached in treatment, and shows the freedom from danger, under properly

guarded conditions of such extremities if they become necessary. No exacerbation of her disease was caused by the high carbohydrate feeding within the period covered. What might have happened had the diet been continued cannot be said, though it is noteworthy that the next case to be described behaved analogously for the same period of time, and then developed a sharp exacerbation while still under the forced feeding. It is possible that the strong tendency toward retention of nitrogen which psoriatics show was a factor which added to the difficulty of treatment. It should be added that joint cases which recover along these lines acquire in most instances an increased tolerance for food if they adhere carefully to their regime. This is beyond question, and is possibly an added reason for the tolerance shown in the experiment last recorded, since she had been upon a limited intake of carbohydrate for twelve weeks, and was almost perfectly well at the time. Properly to test the effect of carbohydrate her maximum intake when well should have been exceeded by a much greater margin, but this was hardly possible of accomplishment. On January 21, 1916, this patient was apparently in robust health, weighing 122 pounds, eating much more generously, and walking on some days as much as eight miles. It is interesting to note that throughout her illness at the hospital she had, and still has, a carious molar tooth, which cannot be ignored as a possible source of infection. Her recovery in spite of this is in keeping with other such instances already cited.

CASE XXXVII.—Fred M., aged thirty-nine years, referred by the courtesy of Dr. A. H. Gerhard, was admitted April 24, 1915, and discharged July 9, 1915. An arthritis of fourteen months' duration involved the shoulders, elbows, wrists, hands, knees, and feet, and incapacitated him. A probationary house diet yielded 2078 calories. He was given a mixed diet of 1268 calories, on which he showed slight improvement. This was changed on May 15, 1915, to 1065. He developed tonsillitis on May 25, after showing evident improvement, and was held back somewhat. By June 15 he was in very good shape, and a feeding experiment with carbohydrate was begun. He was put on a diet of graham crackers 60 gms., apple 150 gms., and weak tea with 7 gms. sugar, three times a day, yielding 1072 calories. On June 20 he got 322 gms. of candy, equivalent to 300 gms. of cane-sugar, distributed during the day. This added 1200 calories, making a total of 2272. On June 24, 40 gms. of cornstarch and 35 gms. of cane-sugar were added to the intake daily, cooked with water and a little vanilla, and making a bulk of 546 gms. This yielded in all 2572 calories. The notes follow:

June 26. For the first time since the forced carbohydrate feeding he seems to have more pain, chiefly in both wrists. Left knee slightly stiffer.

June 27. Says he felt worse when he woke up today than for some time past. At 5 P.M. has increased pain in both wrists, left little finger, left thumb, left ankle, shaft of left arm, and left knee.

June 28. Worse. Points of soreness are right side of chest posteriorly, right side of neck, right knee, left shoulder, both wrists (worse than yesterday), left forefinger, left little finger, left knee, and both ankles.

June 29. Worse. Additional points are the right shoulder, toes, and left pectoral muscles. Diet cannot be pushed further. To return to simple graham-cracker diet tomorrow.

July 1. Has made undoubted progress and is better considerably today at eleven points.

July 3. Right and left little fingers and both wrists are somewhat worse. Right knee shows effusion. Other points are better or well.

July 5. Effusion less. Distinctly better elsewhere.

July 8. Progress satisfactory but not yet back to his condition before the experiment. He grew very tired of the diet and was returned, on July 7, to a mixed diet of 1072 calories. Sent home with instructions to follow the diet for the rest of the summer and report in the fall.

In this case there could be no doubt of the exacerbation induced by the forced feeding. The man was made almost worse than he had been at any time. Also, he had had no prior exacerbations of a nature to be confusing. It is interesting to note, as mentioned in the last case, that these two cases happened to be carried through on exactly the same dates, and that the present case had hardly begun to have symptoms—had certainly shown none that were definite—by the date upon which the former had to be taken off her forced diet without having shown an exacerbation.

Reference is omitted to several other cases under treatment at the present writing.

OBSERVATIONS ON THE HYDROGEN ION CONCENTRATION OF THE URINE AND THE CARBON DIOXIDE TENSION IN THE ALVEOLAR AIR. As already referred to in the text, observations have been conducted in some cases of this series on the hydrogen ion concentration of the urine, as a measure of the true urinary acidity. The methods followed were those developed by Henderson and Palmer,<sup>5</sup> and depend upon the comparison of diluted urine, to which an indicator has been added, with a series of flasks of prepared solutions. These solutions contain weighed amounts of the sodium and potassium salts of phosphoric and acetic acids, and correspond to definite concentrations of the hydrogen and hydroxyl ions, which, in terms of physical chemistry, express acidity and alkalinity. The notation used signifies the logarithm of that number which

<sup>5</sup> Clinical Studies on Acid Base Equilibrium and the Nature of Acidosis, Walter W. Palmer, Lawrence J. Henderson, *Archives Int. Med.*, August, 1913, xii, 153-170.

expresses the actual acidity or alkalinity. The logarithm decreases as the acidity increases, and *vice versa*, and the minus sign is here omitted.<sup>6</sup>

A study of the figures shows that until the patients were placed upon the standard graham-cracker diet no characteristic reactions could be discerned, although the urines in disease and convalescence were contrasted. Cases in apparently comparable stages of the disease gave varying results, and the same case at the same period sometimes showed variations from marked acidity to marked alkalinity.

The samples were from twenty-four-hour specimens, preserved with toluol and kept on the ice. Doubtful ones were discarded. Occasionally, "stat" specimens were also examined. Space will not permit of giving the figures for the cases which were not placed upon the standard graham-cracker diet.

The first case examined upon the standard diet was in Case XXXV. The urine showed the same indefinite variation on the probationary house diet, and when the patient was convalescent on it, but when he was convalescent on a constant mixed diet it approximated stability of reaction. Around January 10, it showed an interesting drop from an acidity of 6 or thereabouts to one of 7.7, a difference of 4.5 in the scale of eleven flasks, from which it slowly recovered. Coincident with this was an exacerbation of his arthritic condition, the urinary change slightly anticipating the attack. This was repeated sufficiently often in this and other cases to suggest that it is a feature of such disturbances, and reflects a metabolic change whose nature is not yet clear. In two instances it led to the anticipation of otherwise unsuspected oncoming attacks, but sometimes appeared immediately afterward. These changes can be seen by consulting the appended tables, and occurred as follows: Case XXXV, as recorded above and again accompanying an exacerbation on January 24. Again on February 19, accompanying an attack produced by carbohydrate feeding. Case XXXIV, on January 11, accompanying an ephemeral exacerbation in one hip and about January 26, accompanying an exacerbation induced by carbohydrate feeding. There was one isolated drop in the acidity on January 6, which was accompanied by no noteworthy symptoms and cannot be explained. It may have been due to an error in the collection.

Case XXXVI showed a less constant reaction during the period observed on the basal cracker diet, owing probably to the error of feeding asparagus which necessarily varied in quality, water

<sup>6</sup> It should be here stated that the logarithmic figures do not portray graphically the differences in reaction of the urine, as a drop from No. 7 to No. 4 in the scale of eleven flasks, three members of the series, is indicated merely by the change from 6 to 7 in the logarithm. This should be borne in mind by those unfamiliar with the notation.

content, etc., and it is interesting to note that the high carbohydrate feeding *per se* made no great change in the hydrogen ion concentration during the period observed. This is in keeping with the observations of Blatherwick on the effect of the ash in diets, and additionally suggests that the change in the cases of induced exacerbation depended upon the systemic disturbance. Owing to the failure to induce an exacerbation the figures are omitted to save space.

Case XXXVII showed the same reduction beginning around January 25, coincident with an attack induced by forced carbohydrate feeding. In the cases above mentioned, the reaction of the urine did not always return at once to its original level but remained alkaline or less acid for some time. The reaction of the urine depends chiefly upon the relative amounts of the dimetal hydrogen phosphate and the monometal dihydrogen phosphate present. A decrease in the acidity as here found represents in the urine an increase of the dimetal (disodium or potassium) hydrogen phosphate as compared with the monometal (monosodium or potassium) dihydrogen phosphate. The metabolic cause of this urinary change remains a subject for future investigation.<sup>7</sup> The long period required to bring these patients into the convalescent or recovered condition, together with the further period and coöperative difficulties incidental to the induction of a clear exacerbation, seem to warrant the presentation of these cases now.

The urinary findings need corroboration from a longer series before they can be accepted as established and observations are pending to that end.

CASE XXXV.—James N. November 17, 1914. Log. = 6.7. Convalescing on house diet averaging 2170 calories.

November 17. Log. = 5.7. "Stat" specimen. Noon: house diet.

November 18. Log. = 6.3. House diet.

November 18. Log. = 7.4. "Stat" specimen. Noon: house diet.

January 5, 1915. Log. = 5.7. 1663 calories of mixed diet; three days convalescent from a "flare up" in the course of recovery.

January 6. Log. = 5.3. 1663 calories of mixed diet. Very well.

January 7. Log. = 5.7. 1683 calories of graham crackers and milk. Well.

January 8. Log. = 6. 3650 c.c. ditto.

January 9. Log. = 6. 2485 c.c.

January 10. Log. = 6.3. 2100 c.c.

January 11. Log. = 7. 1530 c.c.

January 12. Log. = 6.7. 1120 c.c. Exacerbation on night of January 11, on Blatherwick's diet.

<sup>7</sup> Since the completion of the above work, Wilson, Stearns and Janney have reported an alkalosis after parathyroidectomy in dogs. *Journal of Biological Chemistry*, November, 1915.

January 13. Log. = 7.7. 910 c.c. Still sick and effusion in knee.

NOTE.—To test the effect of varying the volume as a possible contributory cause of this difference, the urines of Cases XXXV and XXXIV were diluted in varying amounts up to 100 and 300 per cent. greater volume respectively, but gave the same figures. Except where specified, the specimens were taken from twenty-four-hour collections.

January 14. Log. = 6.3. 1980 c.c.

January 15. Log. = 5.85. 1800 c.c. Well.

January 16. Log. = 5.85. 1840 c.c. 2649 calories started yesterday.

January 17. Log. = 6.3. 2190 c.c. 1827 calories started yesterday at lunch. Now on low proteid diet of graham crackers.

January 18. Log. = 6.2. 1080 c.c.

January 19. Log. = 5.85. 1960 c.c.

January 20. Log. = 6. 2390 c.c.

January 21. Log. = 6. 1870 c.c.

January 22. Log. = 5.85. 1110 c.c.

January 23. Log. = 6.85. 1780 c.c. Well.

January 24. Log. = 6.5. 2160 c.c. Exacerbation last night.

January 25. Log. = 7. 1790 c.c. Effusion in knee still left.

January 26. Log. = 7. 2000 c.c. Well; some effusion still left.

January 27. Log. = 7. 1930 c.c. Well.

January 28. Log. = 7. 2300 c.c.

February 14. Log. = 6.3. 1810 c.c. Graham-cracker diet 1827 calories. Very slight attack in one joint. Began 6 A.M. Gone by noon, almost.

February 15. Log. = 6. 1530 c.c.

February 16. Log. = 6.15. 1810 c.c.

February 17. Log. = 6.7. First urine after candy feeding. 1820 c.c.

February 18. Log. = 6.3. Below par.

February 19. Log. = 7. 1100 c.c. Sharp attack. No effusion.

February 20. Log. = 6.85. 700 c.c. No breakfast or dinner yesterday. Candy stopped yesterday.

February 21. Log. = 5.85. 660 c.c. Practically well.

February 22. Log. = 5.85. 1600 c.c. Well.

February 23. Log. = 6. 1620 c.c.

March 6. Log. = 5.7. 2420 c.c. Mixed diet of 1512 calories started February 23.

March 7. Log. = 5.7. 1880 c.c.

March 8. Log. = 5.6.  $\frac{1}{2}$  1360 c.c. Fever today; joints worse; patient caught "cold."

March 9. Log. = 5.85. 1730 c.c.

March 10. Log. = 5.5. 1590 c.c.

CASE XXXIV. (Mrs. S.) November 17, 1914. Log. = 5.7. House diet averaging 1892 calories.



- November 17. Log. = 5.7. "Stat" specimen at noon.  
 November 18. Log. = 6.  
 November 18. Log. = 5.2. "Stat" specimen.  
 January 5, 1915. Log. = 5.7. Well.  
 January 6. Log. = 7.  
 January 8. Log. = 5.85. 410 c.c.  
 January 9. Log. 6.5. 800 c.c. Comparison not good. Exacerbation in hip.  
 January 10. Log. = 5.85. 700 c.c. Diet of 1089 calories of graham crackers and three glasses of milk begun today at breakfast.  
 January 11. Log. 7.7. 1000 c.c. Exacerbation in hip better.  
 January 12. Log. = 5.3. 380 c.c. Well.  
 January 13. Log. = 5.85. 330 c.c.  
 January 14. Log. = 5.5. 460 c.c.  
 January 15. Log. = 5.5. 300 c.c. Well.  
 January 16. Log. = 5.5. 420 c.c.  
 January 17. Log. 5.5. 410 c.c.  
 January 18. Log. = 5.5. 520 c.c.  
 January 19. Log. = 5.5. 410 c.c. Candy started with 66 gms. of cane-sugar b. d. 528 calories per diem; total calories 1617.  
 January 20. Log. = 5.7. 610 c.c. Menstruating.  
 January 21. Log. = 5.85. 630 c.c.  
 January 22. Log. = 5.5. 280 c.c. Costive.  
 January 23. Log. = 5.7. 530 c.c.  
 January 24. Log. = 5.7. 315 c.c.  
 January 25. Log. = 6. 530 c.c.  
 January 26. Log. = 5.85. 350 c.c. Induced exacerbation.  
 January 27. Log missing. 510 c.c. Candy stopped on January 26.  
 January 28. Log. = 6.7. 660 c.c. Better, but distinctly sore. Effusion in elbow bursa.  
 January 29. Log. = 5.85. 550 c.c.  
 CASE XXXVII (Fred M.).—June 16, 1915. Log. = 5.5. 500 c.c. On graham-cracker diet of 1072 calories. Urine scanty and full of urates.  
 June 17. Log. = 5.5. 810 c.c.  
 June 18. Log. = 5.7. 460 c.c.  
 June 19. Log. = 5.6.  
 June 20. Log. = 5.5. 300 c.c.  
 June 21. Log. = 5.5. 310 c.c.  
 Beginning yesterday got 300 gms. of cane-sugar daily, 1200 calories, or 2272 calories in all.  
 June 22. Log. = 5.6. 360 c.c. Not quite so well.  
 June 23. Log. = 5.8.  
 June 24. Got additional 300 calories from cornstarch and cane-sugar.  
 June 25. Log. = 5.8. 350 c.c.

June 27.	Log. = 5.85.	280 c.c.	
June 28.	Log. = 6.3.	450 c.c.	Exacerbation.
June 29.	Log. = 6.2.	570 c.c.	
July 1.	Log. = 6.4.	340 c.c.	Somewhat better.
July 2.	Log. = 6.4.	340 c.c.	
July 3.	Log. = 6.4.	320 c.c.	Worse.
July 4.	Log. = 6.2.	320 c.c.	Slightly better.
July 5.	Log. = 6.3.	320 c.c.	
July 6.	Log. = 6.2.	315 c.c.	Doing well.

In view of the urinary changes recorded above, and with a view to throwing light on a possible acidosis as well as for other reasons, observations were conducted on the carbon dioxide tension of the alveolar air in several of these cases during ill health and convalescence.

Higgins's<sup>8</sup> adaptation of the Plesch method was employed, using 1000 c.c., as suggested by Boothby and Peabody.<sup>9</sup>

The analyses were made with a Tutweiler mercury gas burette as modified and used by the United Gas Improvement Company of Philadelphia.<sup>10</sup>

Comparisons were first made of the results obtained by using 1000 c.c. of air, and by the exhalation method, the former being finally selected as less variable, though the difference was not great, as pointed out by the above authors.

As seen by the accompanying tables the normal cases undoubtedly averaged slightly higher than the arthritis cases, but while this is suggestive, the difference is not greater than may possibly be accounted for by the fuller diets of the normal cases. Further observations are pending on this point. It is interesting to note, however, that T. K., with active arthritis and on a house diet, had low figures. Fred. M., Case XXXVII, while convalescing on 1072 calories of a graham-cracker diet, averaged less than 32.06 mm., and during an induced exacerbation getting 2572 calories daily of nearly pure carbohydrate, gave an average of only 40.5 mm.

Case XXXVI, Miss C., gave low figures throughout, although at the time getting 2054 calories, supplied chiefly by graham crackers, fat, and whisky. When getting nearly 1000 calories more than Case XXXVII she gave even lower figures than he did. It is evident, therefore, that the conclusion to be drawn at the present writing is that there is no great change of the alveolar carbon dioxide tension characteristic of rheumatoid arthritis. There may be one of minor degree, but further observations are necessary to establish this point.

<sup>8</sup> The Influence of Food, Posture and Other Factors on the Carbon Dioxide Tension in Man, *Am. Jour. Physiol.*, April 1, 1914, xxxiv, No. 1.

<sup>9</sup> A Comparison of Methods of Obtaining Alveolar Air, *Archives Int. Med.*, March, 1914, xlii, 197-506.

<sup>10</sup> The writer wishes to express his marked appreciation to Mr. George H. Fulweiler, chief chemist of the United Gas Improvement Company, for courtesy and assistance in this connection.

## OBSERVATIONS ON THE CARBON DIOXIDE TENSION OF THE ALVEOLAR AIR.

## NORMAL CASES.

R. P.:				
May 14, 1915.	41.60 mm. Hg.	12.30 P.M.	Four hours after breakfast.	
May 17, 1915.	41.20	"		
May 18, 1915.	39.41	3.15 P.M.		
May 18, 1915.	41.20	4.30 P.M.		
June 2, 1915.	39.63	7.00 P.M.	Lunch at 2 P.M.	
June 3, 1915.	42.17	10.30 A.M.	Breakfast at 8.30 A.M.	
Michael:				
June 9, 1915.	43.08	5.00 P.M.	Dinner at 11.30 A.M.	
	45.35	"		
J. F.:				
June 15, 1915.	39.66	6.10 P.M.	Lunch at noon.	
Dr. L.:				
June 16, 1915.	39.1	6.00 P.M.	No food since 1 P.M.	
June 16, 1915.	41.00	6.25 P.M.	No food since 1 P.M.	

## ARTHRITIC CASES.

T. K.—In active arthritis and on house diet:

17. K.—In active animals and on house wire.				
June 2, 1915.	34.21 mm. Hg.	5.30 P.M.	Dinner at noon.	
June 3, 1915.	32.94 "	11.00 A.M.	No breakfast.	
Took 200 gms. cane-sugar and juice of one and a half lemon in water at noon.				
	35.03 mm. Hg.	12.15 P.M.		
	36.92 "	12.40 P.M.		
	35.13 "	1.05 P.M.		
	36.37 "	1.30 P.M.		
	36.01 "	1.50 P.M.		
	36.88 "	2.35 P.M.		
	38.02 "	3.20 P.M.		
	37.36 "	3.50 P.M.		
	38.45 "	4.20 P.M.		
June 4, 1915.	37.63 "	4.50 P.M.	Dinner at 12.30.	
June 5, 1915.	36.62 "	10.55 A.M.	No breakfast.	

CASE XXXVI.—Miss C. Doing well. Getting 2054 calories of graham crackers and fat.

June 11, 1915.	30.44 mm. Hg.	4.00 P.M.	No food since 12.15 P.M.	
	32.86 "	5.00 P.M.		
	29.05 "	5.40 P.M.		
June 15, 1915.	30.39 "	4.30 P.M.	Lunch at 12.30 P.M.	
	28.72 "	5.00 P.M.		
June 19, 1915.	33.10 "	9.40 A.M.	No breakfast.	

Average of two experiments.

CASE XXXVII.—F. M. Pretty well on 1072 calories of graham crackers, etc. Some traces of trouble left yet.

June 17, 1915.	29.39 mm. Hg.	4.50 P.M.	Lunch at 12.30 P.M.	
	34.74 "	5.15 P.M.	Breathing too slowly and result too high.	
	32.05 "	5.40 P.M.		
June 19, 1915.	35.35 "	11.00 A.M.	Before breakfast.	
June 28, 1915.	41.17 "	4.00 P.M.	No food since lunch, but is on the forced carbohydrate diet of 2572 calories.	

Distinctly worse:

35.95	"	4.40 P.M.	
40.38	"	5.05 P.M.	

In the studies previously reported were included observations on the urea and non-coagulable nitrogen of the blood in rheumatoid arthritis which gave entirely normal values. In view of the opportunity, however, to make comparisons in this respect between health and disease, observations were begun to that end, but only one was completed in time to be published. Blood was therefore analyzed from other cases, first before treatment and then when they were convalescent or had recovered under treatment.

The first 3 were ill and no opportunity was afforded to get the blood a second time as they left the hospital, but the figures are given as showing further the normal values. The conditions were as previously reported. It is seen that there is no appreciable difference in the blood findings during active arthritis and those taken during the convalescent or recovered period. The analyses were made by Dr. Charles W. Lüders, to whom acknowledgment is due. Since the completion of this work, Folin and Dennis have reported<sup>11</sup> analyses of uric acid and non-protein nitrogen in 5 cases of arthritis deformans among a larger series of gouty and other patients. These writers conclude that: (1) "In gout the blood is almost invariably abnormally high in uric acid, while the other waste products represented in the non-protein nitrogen of the blood are usually within the normal limits. In arthritis also the blood is not infrequently abnormally high in uric acid but most such cases have abnormally high non-protein nitrogen as well. (2) Neither qualitative tests for uric acid in the blood nor quantitative determinations of the uric acid alone can be depended on in the differential diagnosis of gout and other joint diseases. (3) For a differential diagnosis in doubtful cases of gout or arthritis by means of blood analyses the patient must be on a purin-free diet and uric acid determinations must be accompanied by determinations of the non-protein nitrogen (or urea)."

In their series only 1 of the 5 cases of arthritis deformans gave very high values for non-protein nitrogen (104 mgs.) the others being in the neighborhood of 60 mgs. per 100 c.c. blood, but as the figures of these careful workers are at variance with those of the present writer and imply a means of differentiating doubtful cases of rheumatoid arthritis from doubtful cases of gout, it seems well to include here, with the new cases, those already reported, since they illustrate the great uniformity and low values of the findings in a total of 9 cases of rheumatoid arthritis. These 9 instances were in relatively young individuals free from complicating diseases. They all represented clear-cut examples of rheumatoid arthritis and on 3 of them the analyses of ill health were repeated during recovery with practically identical results. These observations were conducted by two sets of observers, and there seems hardly

<sup>11</sup> Archives Int. Med., 1915, No. 4, pp. 16-33.

room for the possibility of error in the technic. The simplest explanation of this discrepancy is that the cases studied by Folin and Dennis may have had some complicating factor.

Old series.		Total non-coagulable nitrogen in mg. per 100 c.c. blood.		Average.	Urea in mg. per 100 c.c. blood.		Average.
Case VIII.	Patient ill . . .	20.2	21.7	21.00	11.2	12.6	11.9
Case IX.	Experiment 1.						
	Patient ill . . . . .	27.8	25.7	26.00	14.7	14.5	14.6
Case XI.	Patient ill . . .	22.6	22.7	22.65	9.3	10.2	9.6
Case IX.	Experiment 2.						
	Patient convalescent . .	27.0	26.4	26.70	12.8		12.8
Case XIII.	Patient ill . . . .	24.6	25.5	25.00	12.0	14.2	13.1
Case XII.	Patient ill . . . .	24.4	25.0	24.70	10.4		10.4

New series.		Total non-coagulable nitrogen in mg. per 100 c.c. blood.		Average.	Total urea in mg. per 100 c.c. blood.		Average.
Mrs. B.	Ill . . . . .			21.80			16.10
Mrs. S. (Case XXVI).	Well . . . . .			32.30			
Mrs. C. (Case XXVII).							
	Improving . . . . .			26.30			
Mrs. S. (Case XXXIV).	Ill . . . . .			28.70	Ill	12.37	
Mrs. S. (Case XXXIV).							
	Well . . . . .			26.20	Well	14.70	
James N. (Case XXXV).	Ill . . . . .			26.07	Ill	12.35	
James N. (Case XXXV).							
	Well . . . . .			28.30	Well	15.70	

DISCUSSION. A review of the foregoing permits of certain general conclusions. In the first place it is plain from the end-results of Series 1 that cases of rheumatoid arthritis treated along the lines of dietary curtailment, as indicated, will, by and large, indefinitely retain the improvement which may have occurred, provided they adhere to the general principles already followed. A number of cases have now been followed for a long time after recovery, the longest period being nearly five years.

In the second place, it is plain from an extension of the method to another and longer series that a large proportion of cases will show a response to treatment, there being 1 instance (Case XXX) in the 37 here recorded where no influence could be observed. In a definite proportion of cases so responding, treatment may be limited by intercurrent conditions and the desired end-result may be modified or entirely prevented. It was prevented in 1 of the cases which responded and remained under observation (Case XXI).

There are also limitations in cases emaciated or bed-ridden, where a curtailment of diet is in itself contra-indicated. Such cases must be improved in nutrition before they can be successfully carried through. In other words, there is nothing in these dietetic measures *per se* which is harmful if carefully watched, but there are advanced cases of rheumatoid arthritis which have gotten to the point where

any serious disturbance of their routine is dangerous to their already precarious health.

In these cases the arthritis can generally be influenced, but perhaps only at the expense of their already broken health. The writer desires to emphasize this. Even in such extreme types, however, something may be accomplished, and the effort is often well worth while if these truths be appreciated. It is also possible that subsequent study may show more types of cases which do not respond at all to these measures, as already illustrated by Case XXX, and the present report aims to present nothing more than the statistics to date. On the other hand, there can now be no doubt of the entire success of these measures in a great number, perhaps the great majority of sufferers from this disease if they be taken in hand early.

The writer wishes to emphasize again that there is nothing here which controverts the general view that many cases are precipitated or perpetuated by foci of infection. If these foci can be removed, such a step is the easiest and quickest way out for the patient. Unfortunately this is not always possible and frequently failure attends repeated effort to that end. However that may be, the most interesting point in this connection is that *cases showing unmistakable and obvious sources of possible infection in teeth, tonsils, or elsewhere, may improve or recover completely upon a dietary régime.* This is now unquestionable. The real explanation is not at hand.

Too much emphasis cannot be laid on the precautions to which attention has elsewhere been called.<sup>12</sup> Furthermore only minute attention to detail will achieve results and repeated changes in the dietaries may be required.

The writer has suggested previously upon several counts that the large bowel is not chiefly or directly responsible for the symptoms, as has been maintained by some writers, and the experience with Case VII bears this out.

As has been elsewhere noted, several cases of the last series showed some beginning improvement upon the regular house diet. The reason is obvious. If the food tolerance of patients happens to be high, as is often the case, the limited intake of the house diet may be helpful. For example, the evening meal at the Presbyterian Hospital in Philadelphia yields on the average only some 400 calories, and consists of a slice or two of bread, a cup of tea or milk, and some stewed fruit. This house diet, however, is rarely sufficient to maintain improvement, as it is too uncertain; and after obtaining an idea therefrom, in these instances, the total calories have been put safely below that level and made to come from con-

<sup>12</sup> The Nature and Successful Treatment of Rheumatoid Arthritis, Internat. Clin., iii, Series 21.

stant sources. In Cases XXXV and XXXVI the improvement which had begun on the house diet was not maintained and changes of diet were necessary. In the limited space at disposal no reference can be made to all the dietary changes in the various cases. The use of calories as a measure of the amount of food is of course for that purpose only and is not meant to imply necessarily any change in the caloric needs of the body.

The after-treatment of these cases is often important. After the arthritis has subsided the weight may be much lowered, and at about that period the writer has been in the habit sometimes of giving cod-liver oil. It is important to maintain the food level fairly constant for some time and to make additions very slowly, watching the result of each one. Orthopedic exercises are generally indicated, but cannot, of course, be undertaken until the patient has become well accustomed to the new level of equilibrium or has begun to gain weight. The question of the low caloric level at which some of these cases have improved, and indeed continued to live, is a large problem in itself, and brief reference only can be made to it. When the writer first published his results, these diets seemed somewhat iconoclastic, but the experiences of Dr. F. M. Allen in the low feeding of diabetics has since shown how eminently safely this can be carried to even a much further point. There is reason to suspect that some cases of rheumatoid arthritis have a lowered necessity for food as compared with most individuals, or at least with the necessity standards as now accepted. Reference has elsewhere been made to the suggestive overlapping of the symptoms of acute inflammatory rheumatism and those in some cases of chronic arthritis. Illustration of this is to be seen in Cases XXIII and XXIV, as well as in some of the exacerbations of Cases XXXIV and XXXV. It is, of course, not to be understood that acute inflammatory rheumatism and rheumatoid arthritis are regarded as identical, but some symptoms of the former may occur in the latter condition, strongly resembling the redness, swelling, pain, and fever of the acute variety. The undoubted improvement shown under dietary measures strongly suggests a common factor in some of these instances.

No drugs were given in the present series except where stimulation was needed, and, on one or two occasions, where treatment was interrupted. It should be stated that the writer has seen a considerable number of other cases to which no reference is made (many of them referred by his colleagues) because they have not been suitable for treatment or have improved upon the removal of the infectious foci, which step has nearly always been advocated where possible. One case, referred by the courtesy of Dr. Wm. G. Spiller, presented a long-standing ankylosis of both hips. It could not be determined that any active process was present or that any specific benefit followed upon treatment, although the

patient chose to keep to his diet, and writes that he feels in better general health.

Case XXXIV was of the type in which the large joints chiefly were involved, and it is interesting to note, as in some others, that the same favorable results were obtained. Multiple fibrous nodules, easily mistaken at times for bony formations, were present in Cases XXVIII and XXIX, and showed striking resolution under treatment.

In chronic cases long upon a fixed diet, attacks of slight nausea, diarrrhea and the like may occur, requiring mild catharsis and temporary suspension of the diet. Such attacks are apt to be accompanied by exacerbations. Also, it sometimes happens that long-standing cases who may do well for as much as six weeks, require further curtailment of diet even after marked improvement has occurred.

It has seemed important to emphasize with the second series a few of the points already mentioned in order to define the limitations and possibilities in these measures. Many minor points have been omitted, but it is hoped that the general principles have been made clear enough to enable others to obtain results. The sequelae of long-standing rheumatoid arthritis are such that they, rather than the actual arthritis, often present the greatest obstacles. It is to be remembered that the arrest of the causative arthritis does not undo the harm done or transform a cripple, and that even after the causative disease is no longer active there are many factors which may be productive of pains and disability. There is no short cut in the treatment of these patients and the lesson to be learned is to begin early in the disease, before deformity has occurred, at which period most gratifying successes may follow. It is also true that some long-standing cases respond surprisingly well and in such the causative arthritis may be arrested.

The results of the feeding experiments, in which out of four attempts upon patients rendered convalescent or well, exacerbations were induced in three by the ingestion of pure carbohydrate, seem pretty definite. The mechanism of this is not yet clear. It may prove referable to a bacteriological or other cleavage in the small intestine, but whether the process begins there and then or later, the end-effects are of a metabolic nature. Observations upon muscular exercise, not mentioned here, support this and also indicate pretty strongly that within certain limits and under certain conditions, a greatly increased food intake may be made possible by marked bodily activity, when this is permissible.

The one unsuccessful experiment with forced carbohydrate feeding above mentioned can be at least partly accounted for, as suggested under Case XXXVI. The human factor and the limited degree to which biological experiments can be pushed under these circumstances introduce great difficulties, and it is conceivable



that had it been possible to ignore them, the same results would have followed here as in the other three instances.

The principle which this article endeavors to point out is that rheumatoid arthritis is often referable to the dietary factors above indicated. The operation of this principle can be appreciated in a large majority of cases where the measures in question are applied and subsidence of the inflammatory process follows to a greater or less degree. This is independent of the question of complete restoration to health which is conditioned by various factors in which chronicity of the disease and its sequelae play an important rôle. As a matter of fact, however, a gratifying proportion of cases can be materially helped, as the above records show, and, in many, arrest of the disease process may take place.

The writer would like to express his obligation in a number of directions: To Dr. Alonzo E. Taylor, for helpful criticism and the use of his laboratories; to Dr. W. S. Newcomet, director of the Roentgen-ray department, for a long series of skilful coöperative studies; to Dr. Damon B. Pfeiffer, director of the pathological laboratory, for his helpful attitude at all times, and to the writer's colleagues on the staff of the hospital, for the use of beds in their wards, and other kindnesses.

Much obligation is also due to Miss Caroline Milne, directoress of nurses; Miss Helen Wallace, chief dietician, and the nursing staff at the Presbyterian Hospital, on the last of whom has fallen the laborious work of preparing the weighed diets.

**CONCLUSIONS.** 1. The general conclusions already published as to the application of a restricted dietary in rheumatoid arthritis find confirmation within the limits indicated in the present series of 19 cases.

2. In cases rendered free, or nearly so, of acute symptoms by dietary means, exacerbations have been caused as an "experimentum crucis," by the ingestion of pure carbohydrate. Upon the withdrawal of this the symptoms have again subsided. The conclusion seems unavoidable that carbohydrate is a factor in the etiology and treatment of many cases of this disease.

3. Contemporaneously with natural or induced exacerbations of the disease there seems to be a tendency for the urine to show a decreased acidity, as measured by the hydrogen ion concentration.

4. Observations on the carbon dioxide tension of the alveolar air in these cases show no great departure from the normal.

5. The non-protein nitrogen and urea of the circulating blood in uncomplicated cases of rheumatoid arthritis, examined both during ill health and convalescence, fall well within the normal range.

## THE SYNDROME OF COAGULATION MASSIVE ET XANTHOCROMIE OCCURRING IN A CASE OF TUBERCULOSIS OF THE CERVICAL SPINE.

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THE following case occurred on the orthopedic service of Dr. Lovett at the Children's Hospital. Through his kindness it is possible for me to report this illustration of a symptom-complex which has been little described in American literature. Its study may serve to shed some light in the future upon similar cases, seemingly obscure, in which an equally characteristic spinal fluid may be discovered.

**CASE REPORT.**—R. B., male, aged three years; birthplace, Boston; hospital record, 5786.

*Family History.* Father, mother, and three other children living and well. Paternal uncle died of tuberculosis of the lungs. No children dead. Mother has had no miscarriages.

*Past History.* Third child, full term, easy labor. Breast-fed for eighteen months. Eczema at three months; cholera infantum at eighteen months; bronchopneumonia during winter. Has always been a weak, inactive child.

*Present Illness.* Began September, 1914. Parents noticed that the child commenced to hold his head in left-sided torticollis. The latter getting increasingly worse, has been accompanied by some feverishness and considerable irritability. Appetite good; bowels regular.

*Physical Examination.* A poorly-developed and nourished child, sick and feverish; head, otherwise normal, held in marked torticollis. Eyes: pupils equal and react to light and distance. No nasal discharge. Throat clear. Teeth in good condition. Chest: fair expansion; no abnormal changes in breath sounds nor in percussion note. Heart: area is normal; sounds of good rhythm, clear, and loud. Abdomen normal, no masses.

*Local History.* Patient stands with a marked left cervicodorsal, right dorsal, and left dorsolumbar scoliosis, with the head tilted to the left and the chin rotated a little to the right. Walks with a very unsteady gait. Lying in bed no facial asymmetry is noted. Considerable elevation of the right shoulder and the inferior angle of the left sternocleidomastoid muscle, especially at the sternal attachment; no contraction of the trapezius. Head held in approximately 60 degrees of left lateral flexion, 40 degrees of anterior

flexion, and 30 degrees of rotation to the right. All joint motions elsewhere throughout the body are free. General signs of old rickets, rather square head, enlarged epiphyses at elbows and knees, prominent abdomen, some outward bowing of the femora and tibiae, slight Harrison's groove, and rachitic rosary.

Reflexes: Knee-jerks present on both sides. No clonus; no Babinski; no Oppenheim.

Von Pirquet reaction, forty-eight hours after admission, human negative, bovine negative.

Urine on admission: reaction acid; no albumin; no sugar; no acetone. Microscope shows urates and few blood cells. Blood on admission: leukocytes, 16,300; polymorphonuclears, 57 per cent; lymphocytes, 43 per cent.

December 3, 1914. Position of the head has gradually corrected itself since admission. Much less tenderness on moving the head. Guards the neck very carefully and will not voluntarily move the head. Temperature has been running a little evening rise, otherwise his general condition has remained fairly good.

December 15. Patient moves his head to the right on suggestion, but still prefers to hold it to the left. In relation to possible intestinal origin of the trouble, child placed on a buttermilk diet. Also taking aspirin.

December 22. Child now holds his head without lateral flexion; can turn with fair degree of ease both to right and left. The right trapezius is held rigid. Aspirin and buttermilk diet discontinued because of digestive upset.

December 24. Marked rigidity of the neck posteriorly. No headache; no Kernig sign present. A lumbar puncture was made; under slightly increased pressure, 10 c.c. of clear yellow fluid with a slight greenish tinge was obtained. Cell count, three per field. Lymphocytes, 88 per cent.; globulin reaction (ammonium sulphate) positive. Upon standing two hours, moderate coagulation. No organisms on smear or blood culture. The removal of the fluid seemed to alleviate the retraction of the neck.

December 28. A second lumbar puncture, not under pressure, shows the same distinctly yellow color. Renewed examination of the child shows a slight remaining left torticollis and dilatation of the left pupil; marked apathy, insensible to the prick of a pin; any real anesthesia impossible to determine. Right side of the body, from the face down, shows weakness. Patient unable to raise the leg, and able only with difficulty to lift the arm. Knee-jerks exaggerated; ankle-clonus present.

December 30. Examination by Dr. J. J. Thomas: Cervical sympathetic paralysis on right side; weakness of sternomastoid; contraction of pupil; narrow palpebral opening and dryness of right side of face. Right arm and chest give suggestion of beginning flaccid paralysis; the right leg gives a suggestion of beginning

spastic paralysis with ankle-clonus. Positive Babinski; exaggerated knee-jerks. No definite anesthesia can be made out.

January 2, 1915. Examination by Dr. Harvey Cushing: Face shows peculiar sardonic smile. The right eye shows narrowing of the palpebral fissure, some inophthalmos, and a contracted pupil. Vasodilatation persists on pinching the right cheek. Diagnosis of right sympathetic paralysis, cervical. Both pupils react to light; ocular movements normal; globes parallel. Ophthalmoscopic examination negative on the left side and impossible on the right side because of contracted pupil. Tongue protrudes in the median line. Body shows peculiar insensibility to pin-prick. There does not appear to be any complete anesthesia. Patient unable to move the right leg; only in part the right arm; deep reflexes easily elicited without clonus; perhaps better on right than on left. Babinski sign positive, both right and left. No abdominal reflex obtained. Positive findings: (1) muscular weakness on right side of body; (2) right cervical sympathetic paralysis.

January 11. New Roentgen-rays of the cervical vertebrae show an evident carious development in the bodies of the third and fourth vertebrae, a condition not noted in earlier radiographs. General condition of the patient shows slow downward progress. Head traction applied. Wassermann reaction negative.

January 18. General condition very poor. Lungs seem to show pulmonary edema; numerous moist rales throughout; no definite areas of impairment. Breath sounds exaggerated but not bronchial. Face shows on the right side marked flushing, plainly demarcated at the midline; left side shows pallor. This is evidently due to the paralysis above noted.

January 25. Despite the frequency and persistency in the pulmonary edema the patient's condition remains about the same, and the child has been, for the most part, very comfortable. He is kept in a sitting posture, which seems to afford some relief.

January 28. Condition today the same until 10 P.M., when breathing suddenly ceased.

DISCUSSION. In this case, the two interesting points are the cervical sympathetic paralysis and the results of the examination of the spinal fluid.

The records of the cases of tuberculosis of the cervical spine admitted to the orthopedic house service of the Children's Hospital from August 1, 1907, to February 1, 1915, reveal the fact that in a total of twenty-three not one shows the paralysis above noted. Of several standard text-books on orthopedic surgery, only that of Tubby<sup>1</sup> mentions the possibility of its occurrence.

This paralysis may result from torticollis *per se*, without changes in the spinal cord.<sup>2</sup> In this case, however, the radiographic demon-

<sup>1</sup> Deformities Including Diseases of Bones.

<sup>2</sup> See Tubby, loc. cit.

stration of lesions in the fourth cervical body supports the assumption of a spinal origin. The syndrome is the result of interference with fibers in the cervical cord running from the cilio-spinal centre.



Roentgenogram of the cervical vertebrae, showing caries in the bodies of the second and fourth vertebrae.

A review of the work of W. Mestrezat,<sup>3</sup> in which the characteristics of the spinal fluid in Pott's disease have been well summarized, will lend differential interest to the consideration of the present case.

<sup>3</sup> Le Liquide Céphalo-Rachidien, normal et pathologique, Paris, 1912.

As quoted by Mestrezat, Foi and Sicard found when the disease was at its height the following:

1. "Xanthochromie," or distinct yellow color, quite pronounced.
2. An abundant coagulation, either spontaneous or found after the fluid has stood for several hours.
3. The presence of albumoses.
4. A greatly increased quantity of albumin.
5. No glycogen or, if present, a very small amount.
6. A striking capacity for hemolyzing the red-blood corpuscles of rabbit's blood.
7. The cell changes are nil, or, if any are present, they are slight.

When the disease has not progressed very far, the following findings:

1. Albumin present.
2. Albumoses present sometimes.
3. The yellow color very much diminished or entirely lacking.
4. No cell changes.
5. No hemolytic properties.
6. Glycogen content not diminished.

Sicard claims the above modifications are characteristic. In his cases, of twenty fluids examined ten were colorless and ten had the distinct yellow color; albumin was always present; in five cases the albumoses were found.

Mestrezat, however, questions whether these changes are not the typical changes of the syndrome of "coagulation massive et de xanthochromie," of which twenty-one cases were collected by him from various sources.

"The syndrome of massive coagulation and xanthochromie" is shown by typical cases or by so-called "cas frustes," which are variants from the usual type. The two main characteristics of the fluid of this syndrome are marked (quite often rapid) coagulability and the distinctly yellow color. The coagulation at times is so marked that the test-tube may be overturned without spilling any of the fluid.

Of the twenty-one cases collected, the first case was reported by Lepine; later cases by Froin<sup>4</sup> (1903) and Sicard,<sup>5</sup> then Babiński, Cestan and Ravant, Verhagen and Dustin,<sup>6</sup> and others. The primary underlying diseases and conditions were the following: meningomyelitis, tuberculous meningitis of cerebrospinal type, Landry's paralysis, compression of the cord by sarcoma, other neoplasms of the cord, pachymeningitis, and Pott's disease.

<sup>4</sup> Inflammations méningées avec réactions chromatique, fibrineuse, et cytologique du liquide Céphalo-Rachidien, *Gaz. d. hôp.*, 1903, lxxvi, 1003; Syndrome de coagulation massive au cours d'une méningite, 1903, lxxxi, 1587.

Syndrome de coagulation massive, de xanthochromie, et d'hémato-lymphocytose de liquide Céphalo Rachidien, *Gaz. de hôp.*, 1908, lxxxii, 1431.

Une sol-distant-paralysie de Landry avec syndrome de Froin, Mal de Pott cervical, *Soc. d. Sci. med. et nat. (Bruxelles)*, 1909, lxxvii, 169.

A resumé of the clinical signs and symptoms of the twenty-one cases is rather difficult to systematize and arrange. However, there is a generally habitual localization of the lesions at the level of the lumbar cord; most often paraplegias, spastic or flaccid, are found combined with sphincter disturbances, sensory disturbances, and sometimes painful subjective phenomena. In short, it is a process meningomyelitic in type, combined with a compression of the lower cord, which may arise from the above-mentioned factors. The symptoms then extend upward, as more of the cord is involved by the pathological changes, and a lumbar cul-de-sac is formed which is shut off from the remainder of the subarachnoid spaces.

Case XVII, reported by Verhagen and Dustin (1909), particularly concerns the subject of this article. Pseudoparalysis of Landry, paralytic and sensory disturbances quite well marked, beginning in the upper extremities, which finally involved the lower. The autopsy showed tuberculous caries of the fourth cervical vertebra making, by means of the pus, a medullary dorsal compression of the cord, and a fibrinous purulent exudate surrounded the whole dorsolumbar portion. There was complete destruction of the lower cervical cord.

Thus this case of tuberculosis of the spine showed a cervical lesion compressing the cord with an exudate involving the whole dorsolumbar portion. This could easily give rise to the two factors which Mestrezat claims are necessary to the production of the typical findings of the spinal fluid of the syndrome, *i. e.*, a closed cavity of the lumbar region and a resulting stasis of the fluid. So by reason of the pathology the symptoms must perforce begin at a higher level and progress downward, being unlike the usual type of case. It seems that in this class the case now being reported should be placed.

A more detailed study of the fluid according to Mestrezat shows:

1. Coagulation immediate and spontaneous or after the fluid has remained standing several hours.
2. Yellow color, "xanthochromie."
3. Increased albumin content.
4. Presence of albumoses.
5. No changes in cell findings.
6. Sugar in variable amounts.
7. Endosmotic non-permeability of iodine and of the nitrates; exosmotic non-permeability of collargol and salicylate of soda.

**PATHOGENESIS OF THESE ABNORMALITIES.** Babinski (1903) explained the cause as hemorrhage; Sicard and Descomps (1908) gave the preference to a transudative origin of the fibrin and albumin found. These authors, without affirming the existence of a closed cavity in the lumbar region, insisted upon small meningeal pockets, whose walls played the role of transudation. On the contrary, Mestrezat insists upon two factors: (1) the existence of a

closed cavity producing stasis of the fluid in which accumulated the elements issuing from the blood by way of transudation or hemorrhage; (2) an alteration, infectious or toxic in type, in the walls of the cavity, which so affects the vessels that a transudative process or small microscopic hemorrhages are created.

That the closed cavity is a factor may be shown physiologically by the non-permeability of the fluids to colloidal metals. Normally in ordinary meningitic cases (Mestrezat) colloidal metals injected in the spinal canal disappear rapidly. From the chemical point of view the existence of a cavity is evidenced by the facts that the albumins and fibrogens are increased, the spinal fluid is at a standstill and is not renewed, as a result of which no absorption of these elements takes place. Anatomically, by autopsies in six cases, a closed cavity has been demonstrated.

The "cas frustes" of the same author show deviations from the usual findings. These are due to the fact that the compression of the cord is not so forceful or that stasis of the fluid is not complete. Such cases lack one or more of the usual changes; thus the yellow color may be absent, or cell changes may be present and coagulability may be diminished.

The origin of xanthochromie, or the yellow color of the fluid in which no red-blood cells occur, is explained by Mestrezat as follows:

1. By serogenic means, as from transudative processes.
2. By hemolytic means, hemoglobin from entirely disorganized red-blood cells. Such fluids must be from a hemorrhage at least three days old.
3. By icteroid means, such as occurs in jaundice, when the spinal fluid shows a yellow color.

The diagnostic value of a fluid with a yellow color, therefore, is that it indicates icterus, minute meningeal hemorrhage, at least three days old, meningeal inflammation with intense congestion, or finally a symptom of the syndrome of massive coagulation and xanthochromie. Of course, this excludes the presence of actual hemorrhage into the canal, as evidenced by a yellow color and the discovery of red-blood corpuscles either macroscopically or microscopically, the "erythrochromie" of Mestrezat. This last is sometimes a manifestation of cerebral hemorrhage (Stewart<sup>7</sup>).

According to Nornic<sup>8</sup> (1913) the cause of xanthochromie has not yet been determined. He questions whether it is due to the passage of blood pigments through uninjured bloodvessel walls or is caused solely by many small hemorrhages. Schrütznler claims the coloration comes not from blood pigments, but from color derivatives classed under the general group of luteins. The syndrome has been called by the Germans, "Kompressions Syndrome," Kleiberger, Rundfleisch, Erb, etc.

<sup>7</sup>The Diagnosis of Nervous Diseases, London, 1914, chap. XIII.  
<sup>8</sup>Deutsch. Ztschr. f. Nervenhe., 1913, xlvii, 136.



In relation to the pathogenesis of the xanthochromie it is interesting to note the observations of Babes<sup>9</sup> (1914) in asystoliques (patients afflicted with a condition of the heart such that it is unable to make a complete systole, or a systole sufficient to expel the blood from the ventricles). In the examination of 10 cases, 8 showed a distinct color, 2 a less distinct; none of the patients had icterus, spinal fluids of all were negative to reaction for bile pigments. After examining these patients he then observed about 50 cases, divided into two classes. The first were local affections such as hernias, hemorrhoids, uterine fibromas. The second included more general maladies, as tuberculosis, pneumonia, acute appendicitis, etc. The first class showed no spinal fluids with yellow color, in the second it occurred in 5 cases (2 cases of pneumonia 2 of appendicitis and 1 of tumor albus, none showing any cord lesion, and 3 showing increase in albumin content). He explains the occurrence in the asystoliques as due to stagnation of the blood and to a transudation of the blood pigment through the vessel walls into the spinal fluid. In the second class of cases he thinks it is occasioned by minute capillary hemorrhages or to permeability of the vessels of the choroidal plexus and a consequent hemolysis of the red-blood cells. While these cases are irrelevant to the syndrome under discussion, they are of interest because of the occurrence of the xanthochromie, without the changes in coagulability, in cases showing no cord lesions or any pathological pressure on the cord.

It is my opinion that the case at present reported should be classed under the syndrome on account of the count of three cells to a field, the yellow color, and the presence of albumin, as shown both by the acetic acid and by the nitric acid test, and the slight coagulability. If the objection be raised that the coagulation was not "massive," it can at least be classed as one of the "cas frustes." As additional evidence, there are the Roentgen-ray plates, showing an evident caries of the third and fourth lumbar vertebrae, and the paralysis and sensory disturbances affecting chiefly the right side of the body. No localization pointing to the lumbar region occurs, but it does resemble the case of cervical caries of Verhogen and Dustin. It is to be regretted that no necropsy was permitted. It is a fair assumption, however, that the process in the cervical vertebrae produced a compression of the cord, and as a result the paralysis and sensory disturbances. In addition a closed cavity, a cul-de-sac, occurred and a consequent stasis of the cerebrospinal fluid. In spite of the fact that the Roentgen-rays showed most probably some tuberculous involvement of the lungs, from any

<sup>9</sup> La xanthochromie du liquide céphalo-rachidien, dans d'autres maladies que les hémorragies cérébrales, les affections du nerf rachien et l'ictère. *Compt. rend. Soc. de biol.*, 1914, lxxvi, 671; La xanthochromie du liquide céphalo-rachidien chez les asystoliques, *Rend. Soc. de biol.*, 1911, lxxvi, 313.

clinical evidence, this was not apparently the primary cause of death.

In conclusion, it might be well to quote Mestrezat on the value of the spinal fluid in the diagnosis and prognosis of Pott's disease.

"The examination solely of the cerebrospinal fluid will not assure the diagnosis of Pott's disease. It is, however, valuable for showing a meningeal invasion and revealing a compression, which make a lumbar cul-de-sac, a closed cavity, where the cerebrospinal fluid stagnates. The degree of the observed modifications, their persistence or their disappearance in a case of Pott's disease, permits an appreciation of the importance of the lesion and is a means of following its evolution."

My thanks are due to Professor Harvey Cushing for kindly furnishing me the literature on this subject.

## SYPHILITIC BURSITIS, WITH REPORT OF A CASE.

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SYPHILITIC involvement of the bursæ, either as a secondary or tertiary manifestation, is a rare condition.

The earlier writers, Hunter, Dupuytren, Bonnet, and more especially Crocq,<sup>1</sup> recognized syphilis as affecting bursæ, but the first clear description of the condition occurring in secondary syphilis was published by M. Verneuil<sup>2</sup> in 1873. Later<sup>3</sup> he pointed out that also in tertiary syphilis, various bursæ were sites of gummata.

Moreau<sup>4</sup> reported seven cases of tertiary syphilitic bursitis, which are included in a list of fourteen cases published by Keyes.<sup>5</sup>

Buechler<sup>6</sup> and Trost<sup>7</sup> have reported four cases of early bursal involvement in secondary syphilis. The former also cites three cases of gummata that came under his observation.

A very complete presentation of the subject with a critical review of the literature and report of a case was published by Churchman<sup>8</sup>

<sup>1</sup> *Traité des Tumeurs Blanches*, etc., 1853.

<sup>2</sup> *Gaz. Hebd. de Médecine et de Chirurgie*, 1873, 2s, x, p. 22.

<sup>3</sup> *Loc. cit.*, 1873.

<sup>4</sup> Thesis to Faculty of Medicine, Paris, August 8, 1873.

<sup>5</sup> Syphilis as Affecting the Bursæ, *AMER. JOUR. MED. SCI.*, 1876, lxxi, 349.

<sup>6</sup> *Ueber Bursitis luetica*, *Medicinshe Monatschrift*, 1889, vol. I, 393.

<sup>7</sup> Beitrag zu den Erkrankungen der Gelenke und Schleimbeutel im Verlaufe der Syphilis, *Wiener med. Wochenschr.*, 1889, vol. xxxix, p. 515.

<sup>8</sup> *Luetic Bursopathy of Verneuil*, *AMER. JOUR. MED. SCI.*, 1909, cxxxviii, 371.

in 1909. The literature since has remained silent on the subject until recently when Cones<sup>9</sup> reported a case of syphilitic bursitis in a congenital syphilitic.

From a review of the few cases reported in the literature bursal involvement may occur in either congenital or acquired syphilis, primary in the bursae or secondary by extension from the neighboring bones and joints. Occurring in acquired syphilis the disease may be classified as belonging to either the secondary or tertiary forms.

The former occurs as a transient affection together with the other signs and symptoms of secondary syphilis. It responds readily to specific medication. The latter appears relatively more frequently, and usually manifests itself in the form of a gumma, presenting the same characteristics as gummata elsewhere. It is insidious in its onset and runs an indolent course, terminating in cessation and ulceration if not treated specifically.

Pain appears only when the integument becomes involved, and even then is not a conspicuous feature of the affection. The majority of cases have appeared in the bursae about the knee, *i. e.*, eight out of twelve cases observed by Keyes.

The following case seems to merit publication not only because of its rarity but also because it is the only case thus far reported in which there has been a pathological examination of the lesion together with a positive Wassermann reaction.

CASE.—S. P., female, aged thirty-four years; married; occupation, housework. Admitted to the City Hospital on the service of Dr. E. P. Carter<sup>10</sup> complaining of "swollen knees."

*Family History.* No bearing on present condition.

*Personal History.* Always in good health until one year after marriage, at the age of fifteen. At this time she had a diffuse eruption over her body accompanied by sore throat and loss of hair, for which condition she received internal medication for one month. With the exception of enlarged glands of the neck, which were removed by operation ten years ago, the patient has remained well until the onset of the present trouble for which she entered the hospital.

*Present Illness.* Two years ago the patient noticed a small, hard, round swelling over each knee, which has increased slowly in size to the proportions shown in Figs. 1 and 2. Only during the last few months has she experienced any pain referable to the knees.

Examination showed a hard, indurated, and rather sharply circumscribed painless swelling over the anterior aspect of each knee, about equal size on the two sides. There was no evidence

<sup>9</sup> Luetic Bursopathy of Verneuil, Boston Med. and Surg. Jour., 1915, clxxiii.

<sup>10</sup> The writer is indebted to Dr. E. P. Carter for permission to report this case.

of an acute inflammatory process, and no signs of effusion were present. The tumor was firmly attached to the skin from above and to the patella from below, although it was freely movable over



FIG. 1.—Chronic syphilitic prepatellar bursitis of two years' duration. Patient, female, aged thirty-four years. Primary lesion at age of sixteen years. Knees extended.

the knee-joint proper. Flexion of the knees elicited no pain. Circumference of knees over midpatellar region measured 33 cm. Roentgenograms showed no involvement of the bones.



FIG. 2. Same as Fig. 1. Knees flexed.

With the definite history of a syphilitic infection twelve years ago, the presence of a positive Wassermann reaction in the blood, and the absence of a traumatic factor (housemaid's knee), the syphilitic nature of the swelling was suspected. The tumor on the

left side was removed by operation when it was found to involve the prepatellar bursa and to be adherent below to the patella.

Both microscopic (Fig. 3) and gross examinations showed a typical gumma.

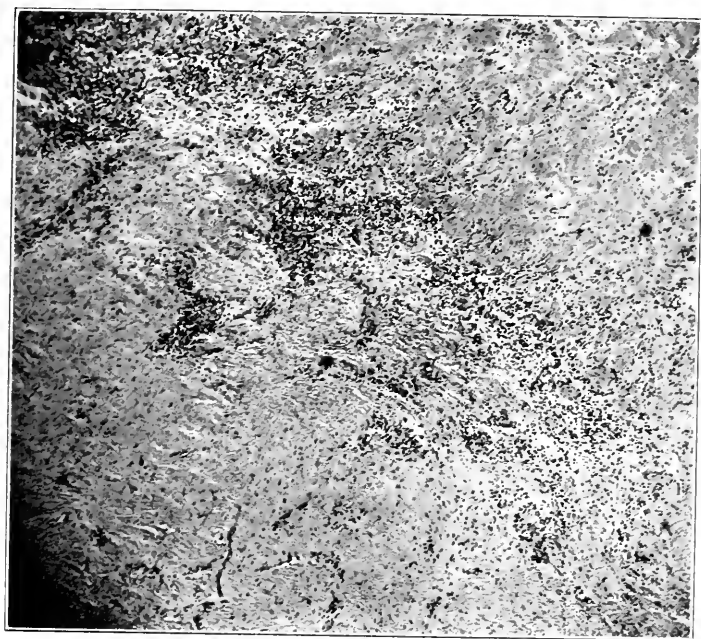


FIG. 3.

The patient was given antisyphilitic treatment for three months at the end of which time the remaining gumma was resolved.

Circumference of knees over midpatellar region now measured  $30\frac{1}{2}$  cm.

## A CONSIDERATION OF CARDIOSPASM, WITH THE REPORT OF A CASE.

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CARDIOSPASM, once thought to be a rare disease or condition, is being recognized much oftener on account of our increasing familiarity with its symptoms and the technical measures necessary to its direct diagnosis.

Only slightly more than a decade ago Mikulicz<sup>1</sup> estimated that about 100 cases had been reported. Since then Gottstein<sup>2</sup> has added 25 additional cases. Bassler<sup>3</sup> speaks of 27 cases that he has treated. Plummer<sup>4</sup> has placed on record 40 cases. Besides these larger series of cases the following additional ones have been published during 1914 by Guisez,<sup>5</sup> Long,<sup>6</sup> Leullier and Guisez,<sup>7</sup> and Reed,<sup>8</sup> and the subject has been treated by Geppert,<sup>9</sup> Heller,<sup>10</sup> Verger<sup>11</sup> and Esehbaum.<sup>12</sup> Geppert's article constitutes one of the best monographs on the subject.

The etiology of cardiospasm is a varied one. Many causes have been advanced and all are doubtless capable of proof in certain cases. The following causes have been suggested:

1. Primary cardiospasm (Meltzer).
2. Primary esophagitis (Martin).
3. Primary atony of the esophageal musculature (Rosenheim.)
4. Functional disturbance of the innervation of the esophagus, due to paralysis of the vagus causing simultaneous spasm and atony of the musculature of the esophagus (Kraus).

5. Congenital disposition (Fleiner, Zenker, Luschka and Sievers).

6. Kinking at the hiatus esophagei (Plummer).

Bassler<sup>13</sup> has recently published an article in which he puts forward the view that cases exhibiting obstruction at the lower end of the gullet of the type which we have hitherto thought to be cardiospasm is not cardiospasm but rather "a spasm of the esophageal opening of the diaphragm due to contraction of the muscular fibers of the crura . . . which contracts the esophageal opening by drawing the central tendon of the diaphragm against the front of the esophagus or contracts it at the sides."

In support of his view, which is based on a dissection of 5 fresh cadavera and Roentgen-ray observations of 7 cases of cardiospasm, he seems able to prove (1) that "the lower extremity of the esophagus or the cardiac orifice of the stomach have no or only a faintly developed sphincter," and (2) that the stricture is almost always epicardial, usually occurring at a distance of one vertebra above the cardiac orifice of the stomach, which corresponds to the esophageal opening of the diaphragm.

<sup>1</sup> Quoted from H. S. Plummer, Collected Papers of St. Mary's Hospital, Mayo Clinic, Rochester, Minn., 1905-09.

<sup>2</sup> Keen's Surgery.

<sup>3</sup> Diseases of the Stomach and Upper Alimentary Tract, p. 829.

<sup>4</sup> Jour. Am. Med. Assn., August 15, 1908.

<sup>5</sup> Bull. Soc. de pédiat. de Paris, 1911, xvi, 141 to 150.

<sup>6</sup> Buffalo Med. Jour., 1913-14, lxix, 403 to 409.

<sup>7</sup> Jour. de méd. de Paris, 1914, 2 s., xxv, 113.

<sup>8</sup> Lancet-Clinic, Cincinnati, 1914, cxi, 378.

<sup>9</sup> Centrallbl. f. d. Grenzgeb. d. Med. u. Chir., Jena, 1914, xviii, 149 to 187.

<sup>10</sup> Mitt. u. d. Grenzgeb. d. Med. u. Chir., Jena, 1913, xxvii, 141 to 149.

<sup>11</sup> Jour. de méd. de Bordeaux, 1914, xlv, 161.

<sup>12</sup> Med. Klin., Berlin, 1914, x, 441.

<sup>13</sup> New York State Jour. Med., New York, 1914, xiv, 9 to 11.

Bassler<sup>14</sup> offers no etiological factors tending to produce this diaphragmatic contraction of the esophageal opening. While his paper throws a new light upon the subject, it would appear to be one concerning proper nomenclature, affecting somewhat the pathology but not altering appreciably the symptomatology or therapy of what we now call cardiospasm.<sup>15</sup>

Under normal conditions we know that food on entering the esophagus requires from seven to ten seconds to pass into the stomach—about one-seventh to one-quarter of this time is required for food to pass down to the cardiac portion of the esophagus, where it remains for several seconds until the cardiac sphincter relaxes and the food is passed into the stomach by the peristaltic contraction of the circular and longitudinal fibers of the esophageal muscles. We have ample proof of this (1) in the Roentgen-ray studies of Kronecker and Meltzer, Cannon and Moser, and others, (2) by the common personal observation of experiencing the sudden aching pain of momentary duration felt back of the sternum in its lower third on swallowing too hot or too cold foods, such as soup, coffee, ice-cream, etc., and (3) by the postmortem evidence, after the ingestion of corrosive poisons, that the greatest amount of erosion in the esophagus occurs at its lower third in the neighborhood of the cardia, where contact with the corrosives has been longest sustained.

While there is this normal delay of foods at the cardia, this varies also with the character of the food, its temperature and chemical concentration, the extremes of all these causing a variable inhibition of the dilating mechanism of the cardia.

Idiopathic or primary cardiospasm occurs frequently, as is seen so often in hysteria and in those of neurotic temperament and tendencies, and is here purely functional; but if of frequent occurrence it permits more and more of the retention of foods, often irritating in character and composition, for too long a time in the neighborhood of the cardia predisposing to the development of esophagitis of varied types, erosions, fissures and ulcerations. Thus a vicious circle is produced, the local inflammation disposing to cardiospasm and the spasm permitting of unduly long retention of foods at the cardia, thereby increasing the esophagitis.

The commonest causes of cardiospasm are *primary cardiospasm* of a purely functional type and constituting a local neurosis, or a manifestation of a general neurosis, and *primary esophagitis*; but when both cardiospasm and esophagitis can be demonstrated simultaneously, it is extremely difficult to decide which is primary and which is secondary.

Of the other etiological factors, congenital disposition may be

<sup>14</sup> Loc. cit.

<sup>15</sup> Heed and Gross in an excellent review of the subject conclude that "cardiospasm is primarily the outcome of a hyperirritability of the vagus." Jour. Am. Med. Assn., January 22, 1916.

an active element in certain isolated cases. Indisputable proof of this, however, should be furnished by the history and the absence of all other etiological factors before one could feel reasonably safe in assigning this as the cause. Likewise, primary atony of the esophagus, while it may rarely occur, is probably also a less common factor in the etiology. Plummer, to whom we are largely indebted for our better understanding of this condition, concludes from a study of his cases that primary atony of the esophageal musculature is a rare occurrence, stating that in his cases "the almost invariable history of spasm at the outset, followed in the later period by the evidence of dilatation—that is, retention of food in the esophagus—is most convincing evidence that the spasm precedes the dilatation and that primary atony is rare." Functional disturbances of the innervation of the esophagus due to the paralysis of the vagus, and kinking at the hiatus esophagei, would also appear to be unusual etiological factors.

**SYMPTOMS.**—There are undoubtedly many cases of cardiospasm so slight as not to give rise to any subjective symptoms and in patients upon whom the diagnosis can be established only by mechanical means. The first subjective symptom usually volunteered by patients is a sensation of discomfort felt behind and usually to the left of the lower end of the sternum. This sensation is variously described as a dull, aching pain, sometimes throbbing, sometimes burning, sometimes cutting or a sense of pressure or weight, as if something had lodged low down in the gullet. These symptoms occur only during the ingestion of food and at first may be of short duration, with periodic remissions, during which the patient is able to eat freely and without dysphagia. During this period the esophageal musculature is sufficiently strong to overcome the spasm and permit of the entrance of food into the stomach with only momentary delay. As the condition progresses compensatory hypertrophy of the musculature must develop to overcome the increasing obstruction, and here a second symptom makes its appearance, namely, the regurgitation of foods from the esophagus into the mouth, very shortly after their ingestion, due to the overactive contracting efforts of the esophageal musculature. The regurgitated foods in this stage may be both liquid and solid, returning in practically the same condition as when eaten and not unpleasant in taste or odor. The majority of the food eaten is passed through the cardia slowly, but nevertheless surely, so long as the hypertrophied muscle proves itself competent to overcome the obstruction. Gradually the muscles tire under their added strain and rupture of the muscle bundles takes place with a resultant dilatation. At this stage the regurgitation of food may be temporarily less frequent and occur at somewhat longer intervals after food ingestion. As the dilatation becomes more extreme the esophageal capacity becomes greater and capable of retention of



larger quantities of food, which are apt to be regurgitated only when the patient is lying down, stooping over, or during a paroxysm of coughing. The dilatation of the esophagus in time may become extreme, with a capacity well over a pint. Since the propulsive power of the esophageal muscle is lacking, food can reach the stomach slowly even when the spasm has been relaxed and in proportion to the weight of the column of food in the esophagus, assisted by gravity. The liquid portion of the meal usually passes more rapidly, seeping through the solid portion so as to leave a dense pultaceous, often foul-smelling mass, usually incorporated with tenacious mucus, which gives rise to a continual sensation of pressure and fulness behind the sternum, with occasional difficulty in breathing, due to pressure on the trachea. As food products are retained for longer and longer periods within the esophagus fermentation and decomposition, chemical and bacterial, take place resulting in secondary esophagitis. At this stage the condition of some patients is truly deplorable; they suffer continually with a sense of burning pressure back of the sternum; they are able to eat only small quantities of food at a time, and their total amount of food ingested and assimilated is so small that they lose weight rapidly; and if not relieved may develop a profound cachexia and die, literally of starvation.

**DIAGNOSIS.** The symptom-complex is usually so characteristic as to suggest the diagnosis, although I must confess that it is not always so easy as it sounds, for in the case here reported I was at first inclined to believe it one of bronchiectasis. The direct diagnosis can always be made by the use of an esophageal bougie, preferably of the Plummer type, very often by means of the stomach-tube or by fleuroscopic study and the Roentgen-ray plate analysis. In the early stages, with the use of the esophageal bougie or of the stomach-tube, it will be found that an obstruction to the further passage of the instrument in adult cases is met with at about sixteen or seventeen inches from the incisor teeth. The instrument can be passed readily until this point is reached, when an elastic-like obstruction is met with, which under firm and steady pressure usually gives way and permits of the passage of the bougie or the tube into the stomach. During the periodical remissions the obstruction will not be met with, or at times the bougie or tube seems about the pass when it is suddenly gripped in the spasm of the contracting muscle which has been excited by the instrumentation. Great care should be practised in attempting to pass the instrument beyond the obstruction, until the diagnosis of cardiospasm is definitely made to the exclusion of diverticuli, a kinking at the hiatus, stenosis due to malignant disease from within or without the esophagus, or from external pressure by an aneurysmal sac or mediastinal tumor.

To rule out these differential possibilities the use of the Roentgen-

ray diagnosis had best be first employed, which will disclose the presence of a thoracic aneurysm, mediastinal growth, the presence of diverticuli, and the irregular outlines of a carcinoma infiltrating the lower end of the esophagus and causing a stenosis. The use of Bassler's cardioplugger<sup>16</sup> will be of aid in securing better Roentgen-ray plates of esophageal conditions. After aneurysm and mediastinal tumor have been eliminated it is safe to proceed with further instrumentation. If either a diverticulum, a kinking of the hiatus esophagei, or a carcinomatous stenosis is suggested by the Roentgen-ray examination it is best to make use of the esophageal bougie devised by Plummer, which consists of a series of olive tips, which are attached to a stout whalebone staff. The olives are perforated from about their middle to the tip. Six yards of thread are then swallowed by the patient, preferably three yards one afternoon and three yards the following morning, which permits of the thread passing well down into the upper coils of the intestines and becoming fixed so firmly that strong traction can be made on the proximal end emerging from the mouth. The olive tip is then passed over this thread, and by means of traction on the thread the olive tip can be safely guided through the cardia. By varying the amount of traction the sound can be introduced into a diverticulum and its depth and size determined.

The diagnosis of cardiospasm may likewise be confirmed by a test which I believe has hitherto not been reported—namely, by esophageal lavage. With the tip of a stomach-tube in the esophagus at a point just above the obstruction, water is allowed to run in from a graduated glass tank. It will be seen to run much more slowly than if the tube were in the stomach. From 100 to 500 c.c., according to the amount of esophageal dilatation, will run in slowly, but evenly until the flow suddenly stops and the level of fluid in the graduated glass tank begins to oscillate slightly. At this point the water is allowed to escape through the outflow tube, and without changing the position of the stomach-tube it will be seen that the amount recovered is equal to the amount introduced. When the capacity of the esophagus has been reached, if instead of opening the outflow tube the fluid is allowed to remain in the esophagus, by its weight, assisted by gravity, it will cause the cardiospasm to relax. This will occur in a varying number of seconds, according to the degree of the spasm, and will permit some of the water in the esophagus to pass into the stomach, thereby allowing an additional flow from the glass tank, which will then usually proceed in a uniform way until recovered by introducing the tube *further into the stomach*. While for purposes of demonstration this latter step may be permissible, it is never wise to distend the esophagus to its point of capacity, as it exaggerates

the already existing atony. The essential point in diagnosis by this method is the ability to recover from the *esophagus itself* an amount of fluid equal, or nearly so, to that introduced. This is not possible of accomplishment in diverticulitis or in stenosis or partial stenosis of the cardia due to pressure from within or without. *It is also of prime importance to determine the presence of a secondary or complicating esophagitis.* This is possible by means of the esophagoscope, but its use is so formidable to the patient that I prefer to make the diagnosis by the examination of esophageal sediments obtained by a method recently published.<sup>17</sup> The photomicrographs used in connection with this paper were made from sediments obtained by this method. It is necessary to determine the extent and kind of this complicating esophagitis because it indicates the proper application of the principles of treatment, *for as long as the inflammatory condition exists so long will the cardiospasm persist*, notwithstanding efforts directed toward the latter to the neglect of the former.

**TREATMENT.** In the earlier cases of cardiospasm of the primary type, relief may usually be obtained by the administration of antispasmodics, such as belladonna and atropin, pushed to the limit of tolerance; and with due regard to a possible neurotic etiological factor, the regulation of proper hygiene, and the use of hydrotherapy and exercise, preferably in the open air, should be advocated. If these measures do not suffice, esophageal bougies may be used or the spastic cardiac ring may be dilated by means of dilators of the types suggested by Plummer and by Bassler. When there is a concomitant esophagitis, measures should be adopted toward allaying this before proceeding to, or simultaneous with, the treatment of the cardiospasm. Suitable measures are the lavaging of the esophagus with medicated solutions best determined and controlled by the character of the esophageal sediment. If the esophageal erosion or ulceration has become secondarily invaded by bacteria one can use germicidal solutions, such as potassium permanganate, silver nitrate, argyrol, etc., until the bacteria have disappeared from the inflammatory desquamation, when blander solutions, such as boric acid or normal salt solution, can be substituted. The use of an autogenous vaccine prepared from cultures grown from the esophageal sediments will facilitate recovery from the severer types of esophagitis. If the esophagitis is sharply localized in the form of ulcerations or erosions, healing medicaments may be directly applied by means of long applicators introduced through a small-bore esophagoscope or through a rubber tube just long enough to reach from the incisor teeth to the lower end of the esophagus. When the condition has progressed to the stage of esophageal dilatation and atony the use of intra-esophageal electricity is indi-

<sup>17</sup> LYON, AMER. JOUR. MED. SCI., September, 1915, No. 3, ci. 402.

cated, preferably with the sinusoidal current or the faradic current by means of a suitable intragastric electrode. The negative pole should be attached to the electrode within the esophagus and the positive pole to the external electrode in the form of a hand sponge, which is to be carried over the transverse processes from the seventh cervical to the third dorsal vertebrae and over the sternomastoid muscles, particularly the left, to stimulate the vagus. Before turning on the current the patient should drink a small glassful of water to serve as a better conductor of electricity and to prevent burning by direct contact. The duration of each treatment should not exceed ten minutes, and should be given daily in severe cases until improvement is noted. In those cases showing progressive loss of weight due to inanition it is important to arrange the diet in the form of liquids, the total caloric value of which for twenty-four hours should be over 3000 calories. This can be accomplished by the liberal use of milk and cream, olive oil, butter, egg-nog, soft-boiled or raw eggs, and non-stimulating broths.

In the very late cases that come under observation during the extreme stage of starvation weakness it is perhaps better to do a preliminary gastrostomy and feed directly through the stomach and try to build up the strength of the patient before proceeding to the other treatments. Apropos of operative procedure, Bassler<sup>18</sup> suggests that "in intractable cases the approach to the site and cause of the stricture had best be made by the safer abdominal route rather than through the thorax, and that an operation which has to do with the division of the crura, either at their insertions or the bisection of two of the inner portions of both at the back of the gullet or some point in the esophageal opening is worthy of consideration."

It is necessary to observe certain patients over a long period of time. Relapses from primary cardiospasm, properly treated, are comparatively uncommon, but relapses due to exacerbations in any residual esophagitis are more frequent. This will be seen in an examination of Chart II.

**PROGNOSIS.** Properly treated patients do well, except possibly those instances of cardiospasm secondary to an esophagitis caused by the action of corrosive poison, which are much more difficult to heal and result in contractions due to scar tissue, which, though healed, may still predispose to spasm. It was my privilege to see 2 such cases in Berlin in Paul Cohnheim's clinic which had been treated respectively for five and nine years.

The following case is reported because it illustrates how stubbornly certain cases may persist when the causative factor is an esophagitis, how relapses are frequent and are due to an exacerbation in the esophagitis and that it is necessary that this should be allayed before the vicious circle of cardiospasm and esophagitis can be broken.

CASE REPORT.—M. J., aged thirty-two years; occupation, piano stringer. Born in Russia.

*Chief Complaint.* The patient first came under observation December 18, 1912, with complaint of "stomach trouble," epigastric pain, morning cough, copious expectoration, and loss of weight.

*Family History.* Negative.

*Past Medical History.* Always well and strong until three years ago, and the only illness he remembers was typhoid fever at the age of eighteen years.

*Social History.* The patient came to America seven years ago, has been married five years, and has two children in good health. Does not use tobacco. Uses light wine occasionally. Denies venereal disease.

*Present Illness.* Beginning about two years ago the patient noticed an uncomfortable feeling of fulness in the high epigastrium with a sense of weight and pressure occurring shortly after his meals, preceded by a slight stabbing pain referred to just above the xiphoid, which would occur irregularly and be associated with the first few mouthfuls of food taken, and would soon pass off to be replaced by a feeling of weight and heaviness. There was no nausea or vomiting but considerable belching, with partial relief and occasionally sour regurgitations. The patient has been steadily losing weight and strength during the past three years. Seven years ago he weighed 205 pounds, and today weighs 144 pounds (subsequently further loss of weight to 128 pounds), and the greater part of this has been lost during the past year.) Two or three months ago he began to be troubled with coughing, and would sometimes spit up a mouthful of very thick, rather foul-smelling sputum, which would seem to suddenly well up in the back of his throat. This had gradually become worse until now, particularly when lying down, and especially when getting out of bed in the morning, he has paroxysmal coughing, which ends with the spitting up of large quantities of thick, tenacious bad-smelling sputum. Of late he has been having night sweats. On some mornings he may spit up as much as a pint and a half of sputum.

*Physical Examination.* Frail, anemic-looking adult male; looks tired out and ill; skin dry and cold.

Eyes negative; no pupillary alteration. Hair, nose, and mouth are negative. Teeth are in good condition. Gums and conjunctivæ are pale. Glands negative. Breath is slightly offensive. Neck negative. *Chest:* long, narrow thorax, with flaring lower ribs. Supraclavicular fossa increased in depth, but equally. Lungs: Tactile fremitus increased at right apex and extends to third rib. The percussion note is dull over this area and particularly at the right posterior apex, where expiration is prolonged, and occasionally accompanied by rales. No sign of cavity formation. Heart is normal in size and position; second aortic sound slightly accentuated; no murmurs; muscular quality deficient.

*Abdomen.* Scars from furunculosis; soft; no distention; no rigidity; no masses; some tenderness to deep palpation one inch below the xiphoid; enlarged area of gastric tympany. Liver, spleen, kidneys, appendix, hernial orifices, genitalia are all negative. Deep reflexes sluggish. Pulse 84, rather low volume and tension; regular in rate; no sclerosis of peripheral bloodvessels. Respiratory rate 20. Temperature 99. Blood-pressure 110-80.

*Technical Examinations.* A stomach-tube passed three hours after a breakfast of scrambled eggs, bread and tea, a cup of coffee, and one glass of water recovered 500 c.c., a dense, tenacious, sour-smelling mass, taking all night to filter to 85 c.c. of turbid filtrate, testing as follows: Free HCl, 20; combined HCl, 25; total acidity 50. Occult blood negative.

In withdrawing the stomach-tube a paroxysm of coughing was induced and was followed by the spitting up of about 200 c.c. of very foul-smelling, purulent-looking material, grayish-white in color and exceedingly tenacious. This material was negative for free HCl.

December 19, 1912. Full dinner last night at 10.30. Now eleven-hour fasting stomach. Stomach-tube shows marked retention of many meat fibers, potato remains, spinach and prune skins. After lavaging the stomach, which required 3000 c.c. to clean, the stomach-tube was slowly withdrawn seven inches, and almost immediately from the end of the tube came about 400 c.c. of foul-smelling, dense tenacious material so mucoid and cohesive as to form a perfect rope, corresponding in size to the lumen of the stomach-tube and which coiled up snake-like in the conical glass receptacle. This material which is identical in appearance with the "sputum," microscopically contains only food rests, desquamated epithelial cells, many leukocytes, and large numbers of bacteria, chiefly streptococci. It is slightly acid in reaction to litmus, but negative for free or combined HCl. This finding, of course, essentially limited the source of this material to the esophagus, but did not differentiate esophageal diverticulitis, stricture, new growth, or cardiospasm. Subsequently it was noticed that at times the stomach-tube, No. 32 French, would pass easily and at other times with considerable difficulty, meeting resistance at a point about 40 cm. from the teeth. The patient was sent to the German Hospital, January 28, 1913, for further study and treatment and remained until June 13, 1913, under the service of Dr. Henry F. Page, to whom I am indebted for the privilege of studying and assisting in the treatment of this patient.

During the time the patient remained in the hospital his pulse-rate varied from 50 to 88. His respiratory-rate varied from 18 to 24 and his temperature from 96° to 100°.

The *sputum* was examined eighteen times for tubercle bacilli with negative results.

*Blood counts* showed a moderate secondary anemia with hemoglobin 77 per cent, on his lowest reading. There was a moderate leukocytosis reaching 15,850, with normal differential counts. Sputum inoculated into guinea-pigs, subcutaneously and intraperitoneally, as well as into the liver, did not noticeably impair



FIG. 1.—The plate from which this photograph was made was unfortunately broken, and it does not show the extent of the esophageal dilatation, which reached up to the first rib. (February, 1913).

the health of the animals which were macroscopically normal when killed and microscopic examination of tissues showed no evidence of tuberculosis or other infection.

*Roentgen-ray examination* of lungs shows a very small area at the extreme apex of right lung in which there is marked increase in density. The remainder of both lungs is apparently negative.

*Röntgen-ray plate and fluoroscopic examination of stomach made by Dr. A. G. Miller, shows moderate peristalsis; the stomach is moderately dilated, the lower border being just below the*



FIG. 2. Shows the recovery of esophageal tonus. Note the excellent peristaltic wave. (October, 1915.)

umbilicus with the patient standing. The bismuth passes slowly into the stomach in a thin but steady stream, but the majority of it is retained in the esophagus and reaches a point level with the first rib, and the width of the esophagus measures from 1.8 to



4.3 cm., at different levels, being narrowest at the point where the esophagus reaches the diaphragm and widest at a point 18 cm. (7 inches) above the diaphragm (Fig. 1). (Cf. with radiographs made twenty-three months later, by Dr. Willis F. Manges, Fig. 2.) There is no evidence of diverticulitis or new growth within or without the esophagus. The Wassermann and Widal reactions were both negative. Esophagoscopy gave unsatisfactory results, nothing further being learned. The patient stood the operation well without the use of anesthesia. Fractional analysis of gastric contents, shows delayed digestion, subacid gastritis and gastric atony. (See Chart I.) Stool examinations were negative.

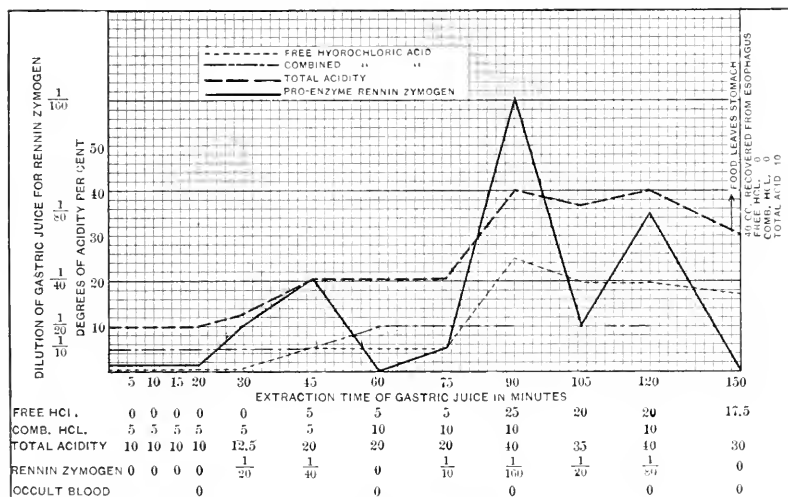


CHART I.—Fractional gastric analysis of Michael Jurzen. The curve demonstrates delayed digestion, associated with subacid gastritis and moderate gastric atony.

The study of *esophageal sediments* repeatedly showed evidence of esophagitis, with marked desquamation of esophageal epithelium, often fragments of epithelium containing from eight to twenty layers of stratified squamous epithelial cells. Many slides examined showed evidence of ulceration, with areas of necrotic debris with large numbers of pus cells; many streptococci and occasional red-blood corpuscles and all manner of food rests. (See Figs. 3 and 4.) These sediment pictures continued during the first few months of treatment with a gradual subsidence in the inflammatory elements, and at present (August, 1915) the esophageal sediments are negative except for occasional exfoliation of stratified epithelial cells. There is too no microscopic evidence of food rests that were such a constant finding during the early months of observation.

The treatment practised in this case was as follows: (1) lavage

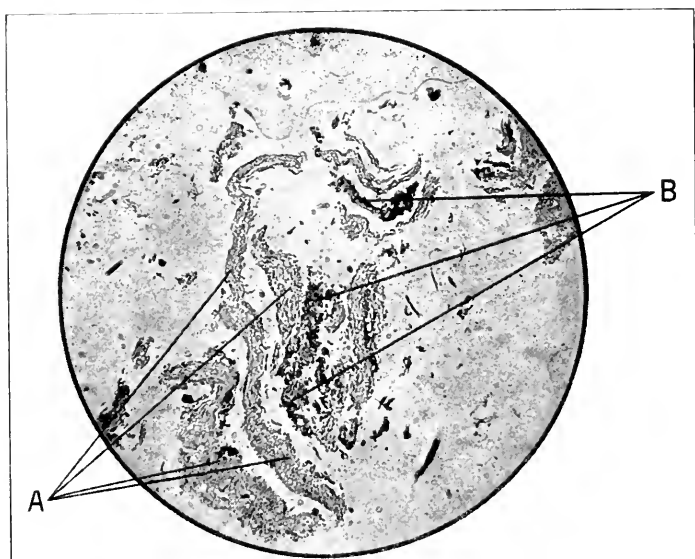


FIG. 3.—Esophageal sediment from a case of cardiospasm. M. J., aged thirty-two years, showing *A*, exfoliated stratified squamous epithelium from esophageal mucosa, with *B*, leukocytic infiltration.  $\times -100$ .

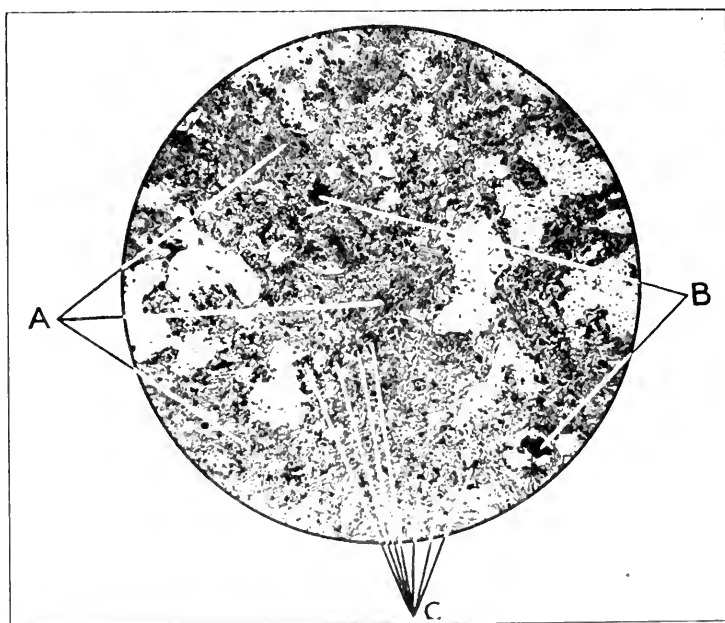


FIG. 4. Esophageal sediment from a case of cardiospasm, with esophagitis. M. J., aged thirty-two years, showing *A*, exfoliated epithelium containing *B*, masses of streptococci, and *C*, leukocytic infiltration.  $\times -100$ .

of the stomach with normal saline or various stomachics, such as quassia, condurango and gentian. After which the tube was withdrawn about seven inches, so that its tip rested in the cardiac portion of the esophagus and the esophageal residual contents were recovered either by simple expression or by being gently drawn off by a syringe. For several weeks the amount recovered each day varied between 200 and 500 c.c., and was very thick, tenacious, and very foul-smelling. (See Chart II.) The esophagus was then lavaged,

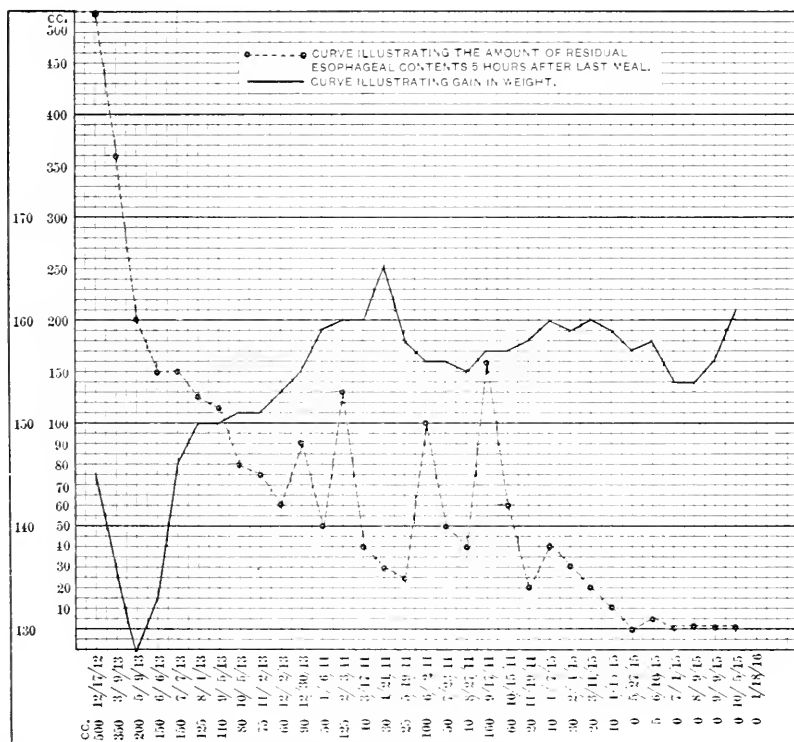


CHART II.—The curves illustrate the decrease in esophageal retention and the increase in body weight as the patient (M. J.) improved.

at first using a solution of potassium permanganate in strength of 1 to 16,000 and 1 to 12,000, until the putrefactive process was under control, and later with solutions of normal salt. During this process of lavaging the esophagus it was found that all of the lavaging fluid could be recovered from the esophagus without having to pass the tube into the stomach. This, I believe, to be pathognomonic of cardiospasm. After lavaging the esophagus, olive-tip bougies, well lubricated, were passed by steady pressure through the spastic cardia, retained in place for several seconds, and then passed

rapidly up and down from four to ten times. At first the tonicity of the spasm was so great as to permit the passage of olive tips, only 5 mm. in diameter, gradually increasing the size to tips 18 mm. in diameter, which can now be passed without effort.

After this an intragastric electrode, properly protected by a perforated hard-rubber tip and a capillary rubber tube, was passed into the esophagus, after the patient had swallowed a glass of water, and the faradic current, and subsequently the sinusoidal current, was used for periods of from five to ten minutes at each treatment. The negative pole being within the esophagus and the positive pole being attached to a small sponge electrode, which was carried over the sternocleidomastoid muscle on either side to stimulate the vagi and over the spinal cord between the seventh cervical and the third dorsal vertebrae. The frequency of treatment was gauged by the amount of the esophageal retention and its character, and by the amount of esophagitis, which was estimated by a study of the esophageal sediments made at frequent intervals. In the first few weeks the amount recovered each day varied between 200 and 500 c.c., and in character was very foul-smelling, and consisted of macroscopic and microscopic food rests, often fermenting, and held tenaciously together by quantities of thick glairy mucus, in which was found microscopically various food rests and many pus cells; stratified squamous epithelial cells from the esophagus, many bacteria, and an occasional red-blood cell. As improvement took place the amount of esophageal retention gradually lessened, and in six weeks had fallen below 150 c.c. Six months later the retention had been reduced to 50 c.c., and gradually became less and less until two months ago (about twenty-two months after treatment was begun), it became impossible to demonstrate esophageal retention of either macroscopic or microscopic food rests.

The *diet* was arranged on a plan of liquid foods of various forms—milk, cream, broths, oatmeal gruel, barley-water, albumen-water, egg-nogs, and olive oil—and was given in small amounts and at hourly intervals, so that the total caloric value for twenty-four hours varied from 3000 to 3500 calories.

Under this plan the patient gained in weight 16 pounds (from 128 to 144) during a period of two months. Gradually his diet was increased to soft and semisolid foods, the latter being gauged by the type of food rests found in the esophageal sediment. His weight is at present 165 pounds, which shows a net gain of 37 pounds. He is on full diet, has no symptoms, and expresses himself as being in better health than he can ever remember, and has been back at his work for about two years.

POLYPOSIS OF THE COLON.<sup>1</sup>

BY HORACE W. SOPER, M.D.,

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COMPARATIVELY few cases of multiple polyposis of the colon are reported in literature. In 1907 Doering<sup>2</sup> collected 50 cases and reported 2 of his own, making a total of 52. In addition to Doering's cases I have been able to collect 8 not heretofore compiled, namely:

Case 1. Dr. P. Y. Tupper.<sup>3</sup> Male, aged ten years. Simple adenomatous polyposis of the rectum and colon. Operation: colostomy; died twenty-eight days after.

Case 2. Esser.<sup>4</sup> Male, aged twenty-nine years. Rectum and colon full of adenomatous polypi. Operation: colostomy at ileocecal valve; recovery.

Case 3. S. Osek.<sup>5</sup> Female, aged thirty-one years. Polyposis of the colon and carcinoma of the rectum.

Case 4. E. H. Terrell.<sup>6</sup> Multiple adenomata of the rectum; diagnosis by proctoscope and treated locally.

Case 5. H. Lillienthal.<sup>7</sup> Female, aged twenty years. Polyposis of the entire colon; rectum free. Operation June 5, 1900. Resection of the entire colon and ileosigmoidostomy; recovery. Patient presented to New York Academy of Medicine January 14, 1901.

Case 6. Z. von Bokay.<sup>8</sup> Child, aged six years. Multiple benign adenoma of the colon. Died two hours after resection of the colon.

Case 7. E. A. Babler and H. J. Niebruegge.<sup>9</sup> Female, aged nineteen years. Carcinomatous polyposis of the colon. Operation: appendicostomy; died nine days after the operation.

Case 8. W. C. Carroll.<sup>10</sup> Male, aged thirty-eight years. Intestinal polyposis. Operation: cecum, ascending colon, and half of the transverse colon removed for multiple adenoma; recovery.

The following is a summary of the analysis of the grand total of 61 cases:

1. The growths are most frequent in children: the ages, however, range from five years to sixty-two years. Twenty-six cases, or 43 per cent., showed the presence of carcinoma. The most frequent

<sup>1</sup> Read at the meeting of the American Gastro-enterological Association, May 10, 1915.

<sup>2</sup> Arch. f. klin. Chir., Band lxxxiii, S. 194.

<sup>3</sup> Paper read at St. Louis Surgical Club, March, 1913.

<sup>4</sup> Deutsches Archiv. f. klin. Med., 1908, Band xciii, S. 535.

<sup>5</sup> Deutsche Zeitschrift f. Chirurg., Leipzig, 1912, cxviii, No. 5, S. 463.

<sup>6</sup> Proctologist, St. Louis, No. 3, p. 158.

<sup>7</sup> American Medicine, April 27, 1901, p. 164.

<sup>8</sup> Jahrbuch f. Kinderheilk., 1913, Band lxxviii, S. 184.

<sup>9</sup> Jour. Am. Med. Assn., April, 1909, No. 16, p. 1235.

<sup>10</sup> Surg., Gynec. and Obst., No. 4, xx, 112.

site was in the rectum, sigmoid, and splenic flexure. Adenocarcinoma was the type of growth in all the cancer cases.

2. The small intestine is rarely involved; the ileum 5 times, jejunum and duodenum 4 times. A tendency for the growths to occur in members of the same family has been observed, notably in the cases of Doering,<sup>11</sup> Cripps,<sup>12</sup> Paget,<sup>13</sup> Smith,<sup>14</sup> Bickersteth,<sup>15</sup> and Zahlman.<sup>16</sup>

3. In 5 cases of benign adenoma, carcinomatous degeneration was observed in various polypi at different places in the colon. The cases of Handford,<sup>17</sup> Petrow,<sup>18</sup> Forster,<sup>19</sup> Doering,<sup>20</sup> Wulf,<sup>21</sup> Hauser,<sup>22</sup> and Bardenheuer.<sup>23</sup>

4. Esser<sup>24</sup> did a colostomy at the ileocecal region. Patient up and about in fairly good health a year later. W. C. Carroll,<sup>25</sup> in the Mayo Clinic, resected the rectum, ascending colon, and one-half of the transverse colon, with the recovery of the patient. Lindner<sup>26</sup> resected the rectum and descending colon, with recovery; the patient was in good health four years after operation. Lillienthal<sup>27</sup> resected the entire colon, performing an ileosigmoidostomy, with recovery.

The case which I present is therefore the second one on record in which the entire colon was successfully resected for polyposis.

CASE REPORT. Male, aged eight years. Came under observation October 14, 1912. He has had a diarrhea since infancy. Two years ago blood appeared in the stool, followed by anal prolapsus. A polyp the size of a walnut was found on the first valve of Houston, removed by clamp and suture by Dr. Ellis Fischel. A second growth in the mucous membrane of the cheek, pea-size, was also removed. Both showed the same histological structure, namely, simple adenoma. The symptoms of prolapsus did not return, but blood persisted in the feces. December, 1912, two pedunculated polypi, hazelnut size, three inches from the anal margin, were removed through the sigmoidoscopic tube by the snare and chromic acid bead cauterization. In April, 1914, four growths, five inches from the anal margin, hazelnut size, were removed in the same manner. Occult blood persisted in the feces, and suspicion was aroused that

<sup>11</sup> Loc. cit.

<sup>12</sup> Transactions of Pathological Society, London, 1882, xxxiii, 137.

<sup>13</sup> Cited by Doering, Arch. f. klin. Chirurg., Band lxxxi, S. 191.

<sup>14</sup> St. Bartholomew's Hospital Reports, 1887, xxiii, 63.

<sup>15</sup> Ibid., 1890, xxvi, 122.

<sup>16</sup> Jahrbuch über die Leistungen u. Fortschritte d. ges. Med., 1903, S. 297.

<sup>17</sup> Transactions of Pathological Society, London, 1890, xli, 133.

<sup>18</sup> Abstract in Centralbl. f. Chirurgie, 1896, S. 542.

<sup>19</sup> Rev. Méd. de la Suisse, Rome, 1903, xxiii, 362.

<sup>20</sup> Loc. cit.

<sup>21</sup> Inaug. Dissert., Kiel, 1892. Cited by Doering, Arch. f. klin. Chirurg., Band lxxxi, S. 191.

<sup>22</sup> Deutsches Archiv f. klin. Med., 1895, lv, S. 129.

<sup>23</sup> Arch. f. klin. Chir., 1890-1, xli, S. 887.

<sup>24</sup> Loc. cit.

<sup>25</sup> Centralblatt f. Chirurgie, 1896, S. 935.

<sup>26</sup> Loc. cit.

<sup>27</sup> Loc. cit.

all the colon might be involved. Abdominal section was determined upon.

Operation, April 18, 1914, by Willard Bartlett. The entire colon was excised. An end-to-end anastomosis was made low in the sigmoid with a Murphy button.

The boy made a rapid recovery. Subsequent sigmoidoscopic examinations showed no recurrence of the growths. His weight prior to the operation was 41 pounds. One year later his weight was 51 pounds. The rectum and a portion of the sigmoid are markedly dilated. At the junction of the ileum with the sigmoid a sort of valve-like fold of mucosa can be seen. The Roentgen-ray examination confirms the sigmoidoscopic diagnosis of dilatation of the rectum and sigmoid.



FIG. 1.—Roentgenogram showing dilatation of rectum and sigmoid.

The small intestine still contained bismuth in the terminal ileum seven and one-half hours after the ingestion of the bismuth meal. He was kept on a diet of soft foods. Raw fruits and vegetables caused several severe attacks of colic, otherwise he has had no inconvenience. The feces are normally formed, one to two movements daily.

The specimen contains eight growths, varying in size from a pea to a small walnut. (See Figs. 2 and 3.)

**PATHOLOGICAL REPORT.** Benign adenoma. The special characteristic is the large amount of connective-tissue formation with cystic dilatation of the intestinal glands. (Dr. D. L. Harris.)

The rectum and sigmoid are involved in 95 per cent. of all cases of polyposis of the colon. Blood in the feces is the predominant

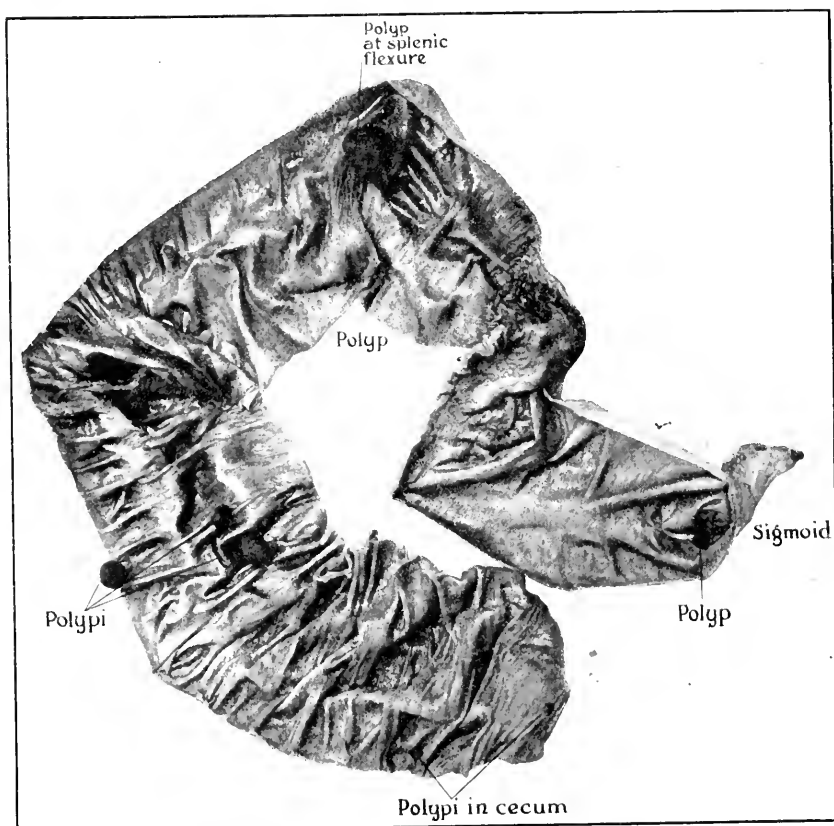


FIG. 2. —Specimen of colon, showing eight polypi.



FIG. 3. —Photomicrograph of section.



symptom and should lead to sigmoidoscopic examination, the only means by which an accurate diagnosis can be made. When limited to the rectum and sigmoid the polypi can be readily removed by means of the snare and cautery, provided they are not too numerous; however, the treatment to be advised is complete resection of the entire colon.

## MYXEDEMA AND THE NERVOUS SYSTEM.

By ROBERT L. PITFIELD, M.D.,

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MOST functional nervous diseases, such as many psychoses and neurasthenias, are not idiopathic, but, like many other disease entities, such as anemia, are caused by infections or intoxications, patent or occult. Tuberculosis, auto-intoxications, or defective secretion or functioning of the polyglandular system are responsible for a large proportion of nervous diseases long considered organic.

It is always wise to explore carefully for the cause of such nervous phenomena. Now that we know that latent tuberculosis plays such an important role, every lesion of the disease, no matter how dry, old, and fibrous it may be, or how long standing, always must be reckoned and appropriately dealt with.

Just so every derangement of the thyroid function plays its part in a causative way. In every physical examination the size and consistency of the thyroid should be observed as regularly as the size and functional ability of the heart is noted.

Most individuals with thyrotoxicosis exhibit constantly many of the stigmata of neurasthenia. Quite a distinct form of psychosis (Basedow psychosis) which may precede any objective signs of the disease, is described by Kraepelin, having hallucinations, mistrust and groundless suspicion, dislikes and jealousies, with tremor of voice and hands.

In athyrosis, quite as often, mental disease of various grades depend upon defective thyroid function. In every case there is nerve weakness, trifling or severe.

Melancholia is the form commonly seen, but acute or chronic manias or dementia may have at least as a large etiological factor, athyrosis.

Perhaps of little moment, but deserving of thought, in adults at least, the skin and appendages, the nervous system, the end-organs of special sense, pituitary and the nervous and chromaffin elements of the adrenal glands, all developed from the ectoderm,

are most influenced by this condition of athyrosis. Any weakness of the skeletal muscle and myocardial insufficiency are probably due to lack of tone depending upon nerve weakness. The exhibition of thyroid extract, the most protean of all medicaments, acts in curious and diverse ways. It increases protein metabolism, and oxidization tends to facilitate the mobilization of sugars; if fed to tadpoles it induces the premature change into frogs, while thymus extract, on the contrary, increases the size without influencing morphology.

It seems to be the potent link which binds through the medium of lateral chains, foodstuffs to starving cells, with "Water, water everywhere nor any drop to drink."

Without it nutritive processes cannot definitely end upon tissues, such as nerve cells, designed to receive such benefactions, but are stored up in fatty and myxomatous masses in the skin. As is well known, overdoses produce all the phenomena of Graves's disease.

Generally in the obese it causes a reduction of fat. In a case of incomplete athyrosis, previously reported, it transformed the nutrition of a thin, nervous, almost cachectic young woman by stirring up her metabolism, into a ruddy, plump, healthy woman. In another case the libido sexualis instead of being increased was obliterated, and remained so after the thyroid extract was stopped.

According to Ewald, notwithstanding the wonderful therapeutic result obtained with thyroid extract in myxedema, even if given up to the limit of tolerance, something yet seems to be needed to bring back absolute mental acuity and well-being in these cases.

In no recovered case of this disease have I ever seen any marked mental vigor distinguish the individual.

The manifestations of athyrosis are as protean as in the action of the extract. It is always accompanied by anemia, nervous depression, and weakness. The fatigability of the individual is greatly increased and other neurasthenic symptoms supervene.

If the mind is strong, with no ancestral psychopathic tendencies, the brunt of the disease is not spent upon the brain but upon the other organs. The anemia may be more marked than the nervous atonia, or the disturbances of the sexual organs in woman may meet the deficiency more than any other parts.

In neurology and gynecology chiefly, athyrosis plays the greatest role; but every specialty has to deal with it just as it has to deal with the other great protean diseases, hysteria, syphilis, and tuberculosis.

Severe cases may resemble pernicious anemia in many particulars; even to the blood picture, the asthenia is marked and anemia profound. Cardiac decompensation and glycosuria, as well as the mental and nervous symptoms above noted, may be induced through athyrosis. Extreme cases are commonly mistaken and treated for dropsical nephritis.

In almost all adult cases the following well-known factors are to be found in their histories. Women who have borne children seem to be affected more than any other class of patients; women who are about the climacteric too are affected more than younger or older women. In many cases, as in exophthalmic goitre, a history of severe infectious process earlier in life, with a probable inflammation of the thyroid gland, is noted. Many have had scarlet fever severely; hereditary syphilis as an etiological cause was noted in several of my cases.

The best results in treatment are obtained in women under forty-five years, after fifty years the results are not as good. The following case, an old abscess of the thyroid body with a resulting puckered cicatrix, probably had destroyed enough of the parenchyma of the gland to diminish the functional requirements and cause myxedema in a single woman, aged forty-four years.

CASE I.—Miss L., aged forty-four years; incomplete myxedema. Since childhood her sister, an intelligent nurse, said she had been peculiar and hard to understand. When about eight years old, she suffered from a severe attack of scarlet fever and diphtheria, and all her ill health dated from this period. Other than this infection there was nothing in her history of etiological moment.

In entering the room I was impressed with this woman's white, immobile, wooden countenance. The cornea of the white eye was the seat of a large scar, and a glance at her throat revealed a deep puckered cicatrix at the site of the thyroid isthmus. An abscess had formed there during scarlet fever and had been opened. She was very deaf. The various stigmata noted at first glance, *i. e.*, the scars and the deafness, all resulted from scarlet fever above noted.

She was a woman of average height and weight, rather slow and deliberate in her movements, with a high-pitched voice common to deaf people.

Her physical condition was that of an anemic woman past the climacteric. Her heart was weak but the lungs were normal. Digestion was good. Menstruation, always regular, began at fourteen years, and had ceased at forty-two years, with hemorrhages at the end. Her blood-pressure was 130; pulse slow and weak. There had been some slight dyspnea, and some edema of the legs and feet. The left kidney was ptosed and painful; pelvic organs were normal, apparently. Her urine was negative. Blood picture: red cells, 4,000,000; hemoglobin, 78 per cent.; polymorphonuclear cells, 62 per cent.; lymphocytes, 36 per cent.; eosinophiles, 2 per cent.

The chief disabilities were nervousness; her station was good; the major reflexes were sluggish. Pupils unequal, due to corneal scar, but responded to light. There was some motor weakness of the legs manifested by early fatigue on standing and giving way of the knees on descending stairs. This is the commonest nervous

symptom in the myxedematous. Occipital headache which was worse on moving her head, also affected her at times.

Her mind exhibited abnormal peculiarities, but hallucinations were absent. She was much depressed, and sat all alone in her home away from her sister and mother. She was jealous of her sisters, and said she believed she was an adopted and not the natural child of her mother. This fixed idea she reiterated again and again to her family. Memory was as good as ever. She felt the cold greatly even in warm weather. She sneezed repeatedly in the sunlight; there was a constant roaring tinnitus aurium.

Her face was myxedematous; the outer half of her eyebrows were thin; her hands were rather clumsy in movements, but delicately formed. Her hair was thin and came out freely; the rest of her skin was normal, save some slight edema of her ankles.

With much difficulty she was persuaded to take thyroid extract. She was told she could not very well get along without it, and having once taken it would procure it herself to relieve depression and other disabilities. More than two grains per diem caused much aching, but on this amount, which she has taken for six months, her depression has disappeared. Her ways are more normal and she is in every way tractable and not despondent. Into her countenance have come lines of expression hitherto obscured by the pad of myxedema. She herself now procures her medicine and depends upon it to keep dispelled the gloom which had so grievously beset her. Her myxedema depended upon a thyroiditis in childhood.

CASE II.—Mrs. von L. is the case of a woman verging near to a definite psychosis, with mental depression of a kind that made her life and that of her family miserable. She was in her late thirties, married, and the mother of one child. Weighed 123 pounds, and was five feet, six inches in height. For five years she was afflicted with occipital headaches, great weakness, and very marked anemia, thought to depend upon uterine hemorrhages, which have been most obstinate.

As a child she was healthy and well. Had typhoid fever at seventeen, but no other severe infection. Began to menstruate at twelve, which was always regular and profuse. She was married at twenty-one; child born in one year after, which was premature by two weeks, and was thin and delicate. Has had many induced abortions since.

Five years ago her health markedly failed. She became nervous. A floating kidney was discovered and a rest cure undertaken, without benefit. Her hemorrhages became profuse, and she was curetted and kept in bed unavailingly. She felt the cold bitterly; even in summer she was chilly and uncomfortable. She was generally confined to the house, cried a great deal, and was greatly depressed from no cause at all.

Physical examination showed a plump woman with white, satiny skin. Her face was that of a sad female given to weeping. Dark, purplish circles were under her eyes. Beyond this her face was expressionless and wooden, with blunt lines. Her hair was thin and patches of baldness were seen. Axillary hair absent. Pubic hair very scanty. There were no pads of myxedematous tissues anywhere on her body except her face. Her skin was thin, beautifully smooth. There was no scaling.

There was no swelling of the thyroid body. It could not be felt. Her throat was edematous and voice coarse and harsh. Speech slow, with a tendency to scanning. Her sight was good for near vision, but far vision was poor. Hearing subnormal, with constant tinnitus in both ears; more marked in a deaf ear. Teeth poor. There was pyorrhea. Lungs were normal; liver and spleen not enlarged. Right kidney palpable. There was tenderness over the appendix and epigastrium. She was always obstinately constipated.

Her heart was dilated to the left. Sounds weak; no murmur or thrill noted. Pulse slow and weak. Legs slightly edematous, and she suffered from substernal oppression on exertion.

Blood-pressure, 108 systolic. Examination of the nervous and muscular systems showed nothing abnormal save great weakness, much headache, and depression. She was exacting and unduly suspicious. If people on passing her house at night were heard conversing or laughing she was sure they were talking about her, and she was most unhappy. Any whispering or conversation in a low tone, so that she did not hear, also affected her in the same way. She was unduly suspicious of her husband, and any waiter or servant in a hotel or house was narrowly watched and undeservedly accused of thieving. She was conscious that these ideas were abnormal, but was so depressed that in spite of her efforts she could not dispel them. She never felt well enough to say "good-morning," although she slept overmuch, and could fall asleep at any time during the day.

Blood examination: red cells, 2,200,000; white cells, 5000; hemoglobin, 52.

Anisocytosis extreme. Marked stippling of red cells and other signs of basophilic degeneration. Degenerated red cells are of significance, in this case probably meaning anemia from other causes than hemorrhages. Uterus and appendages normal in size and position; some endometritis.

Her knees gave way under her, and her gait was described as that of a "twitching hop." She could not walk far without exhaustion.

Under thyroid extract, ten grains a day, she gradually became brighter and her depression and headache very much less; is able to walk more and is not suspicious, and is tractable and agreeable;

indeed, is well. At first she suffered from marked decompensation of the heart on taking thyroid extract, but this finally yielded to rest, Nauheim baths, and digitalis.

The atrophic form of myxedema is well illustrated in the following remarkable case, which was so extreme as to resemble the throes of the last stages of pernicious anemia.

CASE III.—Mrs. P. H., Irish nativity, aged forty-one years, was seen with Dr. Walter H. Andrus. When first treated by her physician she was a withered, bedridden hag, resembling an aged, decrepid woman too weak to leave her bed.

Her family history was entirely negative, with no thyropathic tendencies. Her personal history was the usual typical one of myxedema in woman, in that she was in the fourth decade when the disease began, the mother of four children, born in rapid succession. She also had labored hard and worried very much.

In childhood she had suffered from measles and scarlet fever. In the history of many cases it will be noted that almost invariably the subject suffered from scarlet fever in childhood. Her menses appeared first at fifteen years, and were regular and not painful for years. When she married, at twenty-seven, she was a healthy, active-minded woman of 147 pounds. When thirty-five, after four children had been born, a series of illnesses began to sap her strength, and uterine hemorrhages appeared. Her ambition failed, she became weak and languid, and gave up housekeeping. Occipital headaches now appeared, and for eight years she did not remember a day when she was free from them. Her eyelids became swollen at this time, and her face on arising in the morning presented such a grotesque appearance that she was ashamed to go to the door. Coarseness of the skin and features gradually increased; clumsiness in movements, hoarseness in voice, slowness in speech were evident to all. Her headaches were so severe on rotating her head that she was forced to turn her whole body. Her gait became waddling, and she surely fell if she stumbled. If during the day she was unoccupied for ten minutes she would fall asleep in the chair, with her body dropping forward to her knees. At times when on her knees to scrub she was too weak to rise, and her head would sink to the floor. Her skin became dry and scaly, and her hair fell out abundantly. She could not mount a street car without aid. She was dyspneic on the slightest exertion. Her teeth decayed, broke off, and fell out. At thirty-nine years she took to her bed permanently for her final illness, she supposed, suffering from extreme weakness, aggravated by hemorrhages. Her head had to be supported while she drank and ate. Her vision became dim; she could not distinguish objects across the street.

When seen in 1909 she was bedfast, and on this fairly warm April day she was covered with many blankets and comfortables, and was shivering with the cold. Her weight in the nine years of her

illness had declined from 147 to 118 pounds. Her face presented masses of solid edema, translucent in parts; eyelids looked like blisters, and had to be lifted up by the fingers in order that she might see.

The effort to lift up her eyelids caused deep transverse furrows to appear in her forehead. Her countenance was a "mask of sorrowful fatigue and immobility" (Ord).

Her nostrils were broad and swollen and her lips thickened; the lower one was tremendously increased in size. Over the malar eminences was the characteristic hectic-like flush. The rest of her countenance was of a chalk-like pallor. Her old friends under this disguise of disease did not know her.

Her neck was thin and the thyroid could not be seen or palpated. The rings of her trachea could be seen where the isthmus should have been. There were no supraclavicular pads of flesh; her neck vessels pulsated visibly; her head dropped so that her chin touched her chest. Her hands were broad, clumsy and spade-like. Fingers swollen and very stiff, and could be moved with difficulty. Her legs were the seat of a true as well as a solid edema from weakness of her heart. Hands and feet were always cold and often purple.

A large pad of myxedematous tissue covered and enlarged her abdomen, so that her friends supposed her *enceinte*. Over the middle of the right leg there was also a large pad.

The outer half of her eyebrows was most characteristically devoid of hair, as was the axillary and pubic region. Toe and finger nails were markedly incurved. For years there had been an incontinence of saliva, and every morning a wet spot saturated her pillow. Gums soft and spongy; soft palate edematous and hung down to the base of her tongue. Hoarse croaking of voice characterized her speech, which was scanning in character. Frequently she had to stop in the middle of her sentence to clear her throat. In the open air tears constantly coursed down her cheeks.

Her nervous system was depressed. All voluntary movements were retarded; her apprehension was slow; a marked interval elapsed before she could cerebrated sufficiently to answer the simplest question.

She could sit for hours absolutely still in the same position, as if in a trance, oblivious of her surroundings. For recent events her memory was greatly impaired. Indeed, she could hardly carry a sentence through to completion for sheer lack of ability to remember what she had begun to say. Sleep was heavy and stuporous, disturbed by bad dreams and night terrors; she mostly was placid, but at times displayed irritability, and was cranky and exceedingly disagreeable. Hallucinations of sight were frequent; she saw animals and people "flashing about the room." Tiinitus was so persistent and annoying that when addressed she would put her fingers in her ears to stop the roaring.

Her sense of smell was so deranged that the odor of a dead rat constantly annoyed her, and she insisted many times that her family search for a dead rodent when none was present existed. She declared good fresh food was tainted, and with a bad taste, and would not eat it at times.

Constant chilliness and feeling of cold had been present for eight years. She felt as if cold water was being poured down her spine. When seen about the middle of April, a warm day, not requiring an overcoat, she was in bed with two woolen undershirts, a nightgown, a shawl about the shoulders; about her was a blanket, and over her four layers of blankets, a spread, and a down quilt; added to this her bodily heat had to be augmented by hot-water bottles.

A constant occipital headache she declared was the whole trouble, and felt as if a great weight constantly tugged at her and bore her down. When sitting at the table her head was so oppressed by the painful sense of weight that it was bowed to the table.

Paresthesias affected her hands and feet and rendered her fingers clumsy and useless; she could not thread a needle for the past six years because of the delayed sensation, easily demonstrated. She waddled when she walked (hippopotamus gait); for four years she could not dress herself; she could not recognize a button by touch. Her reflexes were delayed, but otherwise normal.

Her vision was misty, probably from vitreous clouding.

Temperature,  $97^{\circ}$  to  $97\frac{3}{10}^{\circ}$ ; pulse, 80, small and weak; no arteriosclerosis; blood-pressure under 100 systolic; cardiac dulness extended to right sternal line apex fourth interspace nipple line to the left. There was a double murmur at the mitral orifice; slightly accentuated, pulmonary second sound.

Blood examination: Hemoglobin, 25 per cent.; red cells, 2,030-000; white cells, 3400; polymorphonuclears, 40 per cent.; small, lymphocytes, 40.8; large, lymphocytes, 17; basophiles, 1.5; eosinophiles, 0.7; no nucleated red cells, but many degenerated cells.

Sexual desire lost and intercourse was disgusting. Menses always late and profuse.

Urine 900 c.c. in twenty-four hours; specific gravity, 1010; trace of albumin; no sugar; few cylindroids.

Five days after giving her 2 grains thyroid extract, t.i.d., iron, arsenic and digitalis, her headaches disappeared for the first time in nine years; quilts and half of the blankets were removed, and she felt warm and talked more rapidly. At the end of the week her temperature was  $99^{\circ}$ , pulse 100 to 110, and her hands began to perspire.

Patient now was quick to understand, and her voice was more normal; the tones were not so harsh; no swelling about the eyes; no furrows in the forehead; face was thinner and edema gone; natural expression returned; she could thread a needle; bowels more regular.



Pulse rose in ten days to 120, temperature  $99\frac{2}{3}^{\circ}$ . Hands peeling; she could move about. Urine, 1500 c.c. Never slept in the daytime; headaches now gone and felt as if in a dream. No tinnitus; could call downstairs; hearing acute. Itching of skin came on and thyroid diminished. In three weeks patient got out of bed and dressed herself unassisted.

Her thirteen-year-old daughter said that she "never remembered her mother walking and talking like other folks before." After four weeks of treatment with thyroid extract she walked out and was so changed in her appearance that the neighbors did not know her. She speedily resumed her duties in her home as housewife.

After five years she has remained well, under the constant influence of thyroid extract, which has been cruelly denied her through the default of her own gland.

It was as if she had hibernated for eight years and had been incased in some mummifying substance that had benumbed her mind like that of an animal asleep all winter, and had transformed her features into a grotesque mask, and had shiveled her limbs into mere racks whereon to hang her clothes. To add insult to injury, her disease had delicately rouged her prematurely withered cheeks with the bloom of youth. One little vial of a magic medicine such as one reads of in fairy books had transformed the chrysalis into the butterfly and had restored a wife and mother to her family and friends.

CASE IV.—Mrs. G., aged forty-six years, had been ill for years with a multitude of ills culminating in a mild psychosis. This was severe enough to convince three physicians as well as her family that she should be committed to an insane asylum, but this was not done from lack of funds.

She had a family history of psychopathic tendencies. Her mother was somewhat deranged after the menopause and died at seventy-four years.

The chief etiological factors in the production of athyrosis were scarlatina in childhood and the birth of eleven children in rapid succession. She had two abortions also. She was prone to much worrying, and labored hard to care for her large family.

Menses began at sixteen, and were uneventful until after forty, when uterine hemorrhages exhausted her, often lasting ten days, and causing her to keep to her bed. Twice her uterus was curetted to cure this condition, but unavailingly.

She was anemic from hemorrhages and dyspneic on even slight exertion. Her heart was atonic and dilated; her legs were dropsical.

She was a large woman with a waddling gait; weak muscles, which kept her confined to home.

Her nervous system was weak and her reflexes sluggish.

Her mental condition was abnormal in that she was melancholic and depressed; she was unreasonable and incoherent on question-

ing; her mind wandered from the subject of conversation, with no power of concentration at all. She was exceedingly voluble and did not finish her sentences; in fact, could not round out a complete sentence at times. She was given to crying, and would weep for days for no cause. She had the usual occipital headache and subnormal temperature.

Pads of myxedematous tissue covered her abdomen and chest. Her face was wooden-like and expressionless.

The abdomen was so large that she resembled a woman late in pregnancy. Her neck was short, wrinkled, and bull-like.

For five years, even on the hottest days, she had not perspired; her hands and feet scaled and dandruff was in her hair.

Her skin had been wrinkled and yellow for ten years, and her finger nails brittle. Saliva drooled from her mouth and wet her pillow at night. Her lips were swollen and livid; her teeth were decayed and the gums bled easily.

For years she was too dispirited and weak to get up for breakfast. She was dyspeptic and obstinately constipated. Her knees gave way under her and she constantly sought a chair to sit upon.

Here is a large, bloated woman at the menopause, afflicted with melancholy and other stigmata of an ill mind, poor in body as well as in spirit, with a decompensated, atonic heart, having hemorrhages and the attendant anemia, ugly to look upon, a care and bother to her family, grotesque, feeble—a mere hulk. She felt that she would surely die, and no doubt wanted to.

Hardly anywhere in medicine are there any such diverse symptoms or groups of symptoms found all dependent upon one causation factor as in athyrosis. Where, for instance, save in syphilis, do we find such widely diverse components of a symptom complex as a diseased brain and heart coupled with uterine hemorrhages and skin lesions? All such apparently irrelevant symptoms are co-related through the medium of thyroid deficiency.

Hertoghe says that the maintenance of the healthy growth of every cell in the body needs the active function of the thyroid gland.

This woman recovered entirely from her mental depression, hemorrhages, weak heart, grotesque appearances, and anemia through the ingestion of thyroid extract, supplemented with iron and arsenic. She, after five years, is now a useful member of her family circle, and is well.

CASE V.—Catherine G., aged fifty-three years, married, mother of four children, all since dead, was admitted to the wards of the Germantown Hospital suffering from nervous depression and weakness. She was four feet eleven inches in height, and weighed 200 pounds. She suffered from dyspnea and depression of spirits and body, and was confined to her bed for some time.

She could give no account of her parents, and her personal history was meager and unimportant, save that she had always been healthy until of late years.

She never had had scarlet fever or syphilis; at the menopause she suffered from profuse hemorrhages.

Her intelligence was of a low order. A square, wooden countenance, wrinkled forehead, sparse hair, rough skin, spade-like deformity of the hands, bulky of frame, mental hebetude, and depression rendered the diagnosis fairly easy, but it was complicated by a true arterial and cardiac sclerosis. On admission her blood-pressure was 190 systolic and 100 diastolic. Her heart was slightly

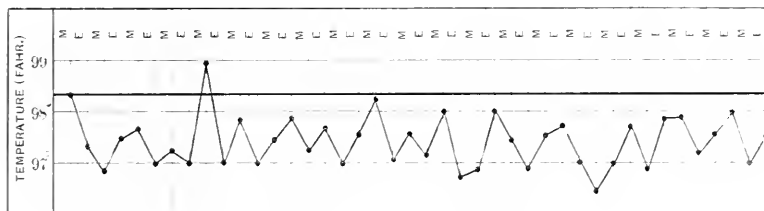


FIG. 1.—Before taking thyroid extract. Average temperature for three weeks, 97° F.

dilated and her legs edematous. Her pulse was 56 and regular, her respirations for days were over 35, and she could speak with difficulty because of this. Casts and albumin were found in the urine; there was polyuria. For five months during her stay in the hospital her temperature was subnormal almost all of the time. Her mind was slow, her memory exceedingly poor, and she could make no new mental associations. Tremor was marked in her hands, and she could not thread a needle or even feed herself at times. Her station and locomotion were good save when she walked it was with the typical hippopotamus gait. Her knees

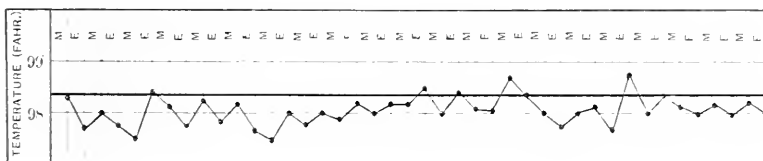


FIG. 2.—After taking thyroid extract, 97.8° F. Average three weeks' temperature, showing increase of 0.8° F.

at times gave way under her and she suffered much from headache. All deep reflexes were prompt and normal, sensation was delayed, at times a lateral nystagnus was seen. Her skin was harsh, dry, hair thin, bags of myxedematous tissue covered her upper eyelids.

In July she sat in bed to keep warm, covered with three or four blankets, complaining that she felt cold. She spoke of a bad taste in her mouth and of tinnitus aurium. While she was very large no distinct pads of myxedema were seen save over her eyes. Her

eyebrows were thin; she wept a great deal, and was manifestly unhappy.

Owing to the administration of too much thyroid extract her heart became more dilated, she became more dyspneic and dropsical, and for a while her auricles went into fibrillation. This decompensation of the heart is often noted in many myxedematous cases in the beginning of thyroid medication. For a long time thyroid extract was given without any benefit, even harm, and finally it was stopped and iodides given freely.

No appreciable improvement had been noted in her condition for eight weeks under thyroid treatment, but there was marked improvement under the iodides. A motor aphasia appeared which further depressed her spirits. A new brand of thyroid was secured, and under a daily dosage of 3 grains her depression disappeared; her heart became stronger and assumed its normal size and rhythm. She began to perspire and to feel warm, and discarded her blankets and walked around the ward with a cheerful mien and disposition. She can thread a needle and also feed herself. She still is somewhat dyspneic, weighs 191 pounds, and is myxedematous. Her tinnitus is gone and her aphasia is much better, but is still manifested by hesitancy in speech when she is anxious to talk and excited. The aphasia was probably caused by some arterial degenerative process incidental to her years; it might never have appeared if her brain had not already been predisposed by her athyrosis.

In every branch of medicine do we meet with manifestations of athyrosis even in those not myxedematous, and every man, particularly specialists in the various branches of medicine, should be alive to this condition.

Not only do neurologists meet with it, but obstetricians and gynecologists have to deal with menorrhagias that are not cured by curetments, repeated abortions, sterility, delayed involution of the uterus toxemias of pregnancy and amenorrhea; but surgeons see bones that will not unite in those with athyrosis.

Mysterious anemias, weak hearts, neuralgias, headaches, glycosurias, precordial pain and distress, nocturnal bed-wetting in children puzzle internists, and unless the true cause is known, baffles them.

Some cases of psoriasis and eczema, milk-crust in children, alopecia, and psoriasis seen by dermatologists and are unamenable to treatment unless thyroid extract is employed.

And the same is true in laryngology; laryngitis, aphonia, tinnitus aurium, even deafness, Eustachian stuffing, and intractable catarrhs depend upon athyrosis. Blepharitis in the aged can be cured with thyroid extract.

Not only must extract of thyroid be used, but iron, arsenic and digitalis combined with rest, massage and Nauheim baths must in many cases be employed in order to increase the amperage of the currents of life in individuals thus afflicted.

A convenient laboratory method for the determination of the thyroid content of the blood, just as hemoglobin is estimated, is needed very much in medicine.

To Dr. Walter H. Andrus, of Germantown, Philadelphia, the writer is indebted for notes of two cases and for the privilege of seeing one of them. To Dr. Harry Harvey also the writer owes his indebtedness for notes, etc., in one case seen with him.

## **FIVE YEARS' EXPERIENCE IN THE TREATMENT OF PULMONARY TUBERCULOSIS BY AN ARTIFICIAL PNEUMOTHORAX.<sup>1</sup>**

BY MARY E. LAPHAM, M.D.,

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IN 1909 the Highlands Camp Sanatorium began the treatment of pulmonary tuberculosis by an artificial pneumothorax according to the principles established by Forlanini, the author and perfector of the method.

The most important points for us have been the determination of the effect of the method upon the contralateral lesions and the decision as to whether these lesions indicate or contra-indicate the method; the pros and cons of delay; the quantity and frequency of the fillings; the amount of pressure; how best to break up adhesions, stop hemorrhages, prevent and treat pleural effusions.

In determining whether the contralateral lesions permit or forbid an artificial pneumothorax, we have to consider whether the condition of the patient is serious enough to warrant the attempt as an *ultimum refugium*; the extent and the nature of the lesions; the probable effect of suppressing the absorption of toxins; the probable effect of increased intrathoracic pressure upon the better lung and interference with its circulation.

We have had two cases come to us as a last resort, perfectly aware that failure and death were far more probable than recovery; both lived for more than two years, possibly because the absorption of toxins from the bad lung was suppressed. Another case with superficial, fine, wet rales all over the better lung in front from the second to the sixth rib; with absence of first sound of the heart and no palpatory apex beat; soft, irregular pulse and decided tendency to intermission; with the upper lobe of the bad, right lung almost entirely excavated, and the rest of the lung full of degenerating foci, offered little hope of recovery from an illness of more than two years in bed. There was marked cachexia, total loss of appetite,

<sup>1</sup> Read at the Meeting of the Tri-State Medical Association, Charleston, S. C.

periodical attacks of temperature of 101° F. The right lung and cavity was compressed without any difficulty; the rales in the left lung disappeared and the heart action improved. The patient is out of bed, comes up quite a hill for his fillings, and promises a recovery.

Another case of extensive rales in the better left lung with similar cardiac conditions was regarded as hopeless. Again, the compression of the cavities in the bad lung was followed by the disappearance of rales in the other and by improved heart action. This patient is earning his living. Neither the physical signs nor the Roentgen-ray encouraged us to hope for results in these four cases, and it was only as a last chance that they were undertaken.

In the last two cases it is possible that the wet rales were caused by the dilating influence of the toxins, and that this was comparable to an excessive dose of tuberculin upon vessel walls injured in their tonicity by the long-continued action of poisons. The Roentgen-ray showed extensive peribronchitic infiltrations of these left lungs together with old scars, but no unmistakable evidences of activity. In these cases the rales indicated leakage through vessel walls rendered more permeable by tuberculins and not degenerative processes. We have had several bilateral cases similarly benefited, so that the extent of wet sounds in the better lung does not seem to us as prohibitive as it once did, provided the Roentgen-ray suggests absence of active lesions. On the other hand, we have had several cases of absence of rales in the better lung, and apparently only scars revealed by the Roentgen-ray, in which the increased functional demands upon the lung or the increase in intrathoracic pressure caused the appearance of rales in the region of the heart, which in spite of all precautions increased and affected the integrity of the lung. In one of these cases there had never been any abnormal breath sounds or rales in the better lung, and the compression of the bad lung had caused the disappearance of the clinical signs of tuberculosis, when a severe nervous shock brought on an edematous infiltration of the better lung, from which the patient never recovered.

If the contralateral lesions are severe it is possible that delay will increase them so that the attempt can never be made and that prompt action is the one chance. We are often tempted to delay, hoping that the lesions will improve and give us a better chance for holding out against the increased strain. We waited for this improvement recently, but by so doing lost the opportunity. We are not able to predict whether these serious cases will be improved or harmed by delay, and it is only the outcome which tells us whether our judgment has been right or wrong. A case of 103° F. temperature with almost daily chills, aching, and other signs of toxemia improved after resting in bed for a year, so that we were not afraid to undertake the compression of the thoroughly bad lung.

The better lung has steadily improved and the prospects are good. Possibly if we had begun sooner the lung could not have stood it. Several times delay has seemed to assure recovery by getting the lung in much better condition, so that a case which was contra-indicated became possible.

In two cases we should have begun the compression a year before we did. In one there was caseous pneumonia of the right upper lobe which we thought would heal without any interference. During the fall and winter the lung was dry and apparently cicatrizing. There was every indication of satisfactory recovery until the warm weather came, and then rales reappeared and a little blood was coughed up, so that it seemed best to compress a lung that broke down so easily. A good recovery was obtained with working capacity, which persists, but if we had compressed the lung when the patient first came to us we would have saved him nine months' time, all the expense, and loss of working capacity, and the consequent discouragement and dissatisfaction.

A second case was that of a small cavity in the lower part of the right upper lobe, which we were confident would heal. The patient gained in every way for eight months, and then severe hemorrhages induced us to compress the cavity. Our mistake is very evident looking back, but we had just begun the work, and our first principle was never to use the method unless compelled to, and so we cost this patient his time and money and a strong sense of impatience and loss of hope. Another case was wiser than we. Told that compression afforded greatest security against loss of time and toward recovery, he preferred taking the chances incident to dangers and be on the safe side, although the chances were in favor of a prompt recovery without the need of interference.

Murphy, in his unbounded enthusiasm, urges the treatment of early cases regardless of the possibility of recovery without it, and compares the condition to appendicitis with all its danger of delay. Forlanini also advises its use earlier than is commonly deemed advisable.

As we learn the ease and certainty of recovery in uncomplicated cases, it seems more and more as if the risks of delay outweighed those of prompt action. If some public sanatorium would furnish statistics from a large enough number of cases treated before the necessity for the method was apparent, we could judge better whether to still advise delay until sufficient harm was done to warrant our interference, or forestall delay and increase the ease of technique by prompt action. We are in favor of regarding earlier cases as indicating the method and of giving it a much wider field than we have hitherto.

For a time we tried to determine the result of a filling by the area of tympany and the absence of breath sounds, together with metallic clinking or breathing and the coin tests. We find that the

area of the pneumothorax can be roughly mapped out by these means, but that the condition of the lung is not revealed. With all the physical signs of a complete pneumothorax the Roentgen-ray may show the sounder portions of the lung well compressed while dense infiltrations remain prominently exposed and uncompressed. Cavities that give no sign are seen to be surrounded by adhesions, and the use of screen or radiographs furnishes the only reliable information. We try to give as few fillings as possible and to use as little pressure. The complete pneumothorax may easily depress the diaphragm, causing insomnia, loss of weight, extreme nervousness, and rales in the other lung. The pressure may be low, even below that of the atmosphere, and yet the diaphragm be too much depressed. If adhesions hold the heart one way and the gas force it another the action is embarrassed. A weak mediastinal pleura may not register any pressure, but nevertheless, the Roentgen-ray shows it forced over until the other lung or the heart is embarrassed. Deep mediastinal pressure may fatally affect the action of the heart if it is a flabby muscle and the danger not be shown by the manometer. The dyspnea is not necessarily great, nor any other marked discomfort. The distress may be vague and ill defined, and the patient suffer more from inability to sleep than anything else. There is nothing in the physical signs to explain the danger, and only the Roentgen-ray shows it. The readings of the manometer are inaccurate guides when the mediastinal pleura stretches and yields instead of raising the pressure.

The breaking up of adhesions seemingly demands higher pressure, but it is possible that too sudden a rise in pressure may account for many cases of pleural effusions, empyemas, perforations, and spontaneous pneumothorax. In judging of a series of cases like Vollhard's it would be interesting to know the pressure and the Roentgen-ray picture. It is safer to give adhesions time to thin out and not to attempt to stretch them too rapidly. If the thick bands are too resistant, or the synechiae around cavities are too dense to separate, cavities may have to be compressed by either breaking up the adhesions by pneumolysis or a thoracoplasty tried. Some very discouraging cases of adhesions with uncompressed portions of the lungs containing cavities have finally yielded to low pressure, persistently maintained by the frequent giving of small quantities of nitrogen without causing enough pull on the surface of the lung to cause a pleurisy or perforation. The same is true of cavities with bleeding vessels. In hemorrhage cases it is necessary to watch the compression of the lung with a Roentgen-ray in order to see whether the vessels in the thick walls of a cavity may not be subjected to a strain which will cause hemorrhage when the rise of pressure cannot compress the cavity but simply changes its shape. Although severe cases of progressive hemorrhages demand severe compression, it is not always safe to use high press-



ure, because the cavity may bleed and also because the pressure from below may increase the congestion of the uncompressed portions and favor hemorrhage. Some hemorrhage cases do splendidly for a certain time, and just as all seems to be over and the danger-point passed, a severe hemorrhage may be aspirated into the other lung and cause death. Even a very small cavity surrounded by compressed tissues may torment the patient by the frequent spitting of streaked sputum. Even when there has been dangerous hemorrhages, and we are anxious there shall be no more, high pressure should be avoided unless the Roentgen-ray shows safety. Again, the readings of the manometer may be misleading by reason of the stretching of the mediastinal pleura and a severe hemorrhage first inform us that a deep mediastinal pressure has altered the shape of the cavity and started bleeding. A case of persistent hemorrhages for six years with advanced bilateral lesions, bled so profusely that he was nearly strangled. Half-fainting and all unconscious of our efforts, he was held up from behind in a sitting position while 800 c.c. of oxygen were given. Oxygen was used because he was so livid and lifeless that we were afraid the heart could not stand the strain, and also because we hoped it would have a stimulating effect by being absorbed. The color came back, the patient revived, and all was well until nitrogen was used, because the rapid absorption of the oxygen did not keep up a steady pressure. Eight hundred c.c. of nitrogen were given and an adhesion pulled out the surface of the lung, a tension pneumothorax developed, and he died. If oxygen had been used and the pressure raised to  $+2$ , the pressure used with the nitrogen, it is quite possible that the increased pressure would have forced a more rapid absorption of oxygen and taken the strain off the adhesion, and there would have been no perforation. We are confident that when the pressure is raised with adhesions, oxygen is safer than nitrogen.

In another hemorrhage case lasting for three days, and frightfully severe, we could get no readings with the manometer. We argued that the lung was stiff and rigid with hemorrhagic infiltrations, and could not be affected by the respiratory movement of the chest wall. We were anxious to prevent any more bleeding by a thorough compression, and considered a Brauer incision, but waited, hoping that the lung would dry out and give respiratory excursions. After two weeks the breath sounds began to be heard faintly over the dull areas, and in a few days more there was no difficulty in obtaining readings on the manometer. The lung was completely compressed without difficulty, and the patient is making a good recovery.

The prevention of pleural effusions depends upon technique and good antisepsis, but even with the best technique it is theoretically impossible, even with a Kjer-Petersen needle, to avoid the carrying in of infection from the deeper layers of the skin. Children coming home from school and filling the house with "colds" or

grippe, or bronchitis, or any other infection, are a good cause of pleurisy from acute infections. Chilling, overphysical strain, overeating, and "bilious" condition, etc., predispose. Infectious pleurisies are common after any acute infection. Static pleural effusions form as the result of too much strain upon the injured vessels; the separation of the pleural surfaces favors the dissemination of tuberculous processes over them. The rupture of a tuberculous focus in the periphery, the forcing of such a focus to the periphery by the collapse of the surrounding tissues; the strain upon adhesions and irritation of the adjacent tissues; the rupture of lung substance and formation of a pulmonary fistula from a cavity to the surface; the pulling out of adhesions and consequent empyemas, are all the result of too much pressure, too hastily applied.

Static and infectious pleurisies demand no treatment beyond that of ordinary pleurisies unless there is too much pressure. As a rule, the pressure rises with an effusion, but occasionally it falls even when the fluid reaches as high as the clavicle. Unless there is some symptomatic indication, rest in bed and the ordinary treatment of a pleurisy suffices; but if the dyspnea becomes marked, or insomnia, or the heart action is wrong, or there are vague sensations of malaise that the patient cannot well define, it is well to remember that an effusion can cause just the same deep mediastinal distress as nitrogen, and that this will not be revealed by the manometer but demands the Roentgen-ray. The effect of the fluid is usually good, sometimes surprisingly so, but there are three conditions that need watching: the expansion of the collapsed lung under the fluid, the penetrating tendency of the fluid and consequent danger of perforation, the conversion of the whole pleural cavity into a cold abscess.

Static pleurisies do not have temperature; infectious pleurisies may have a high temperature and stormy course but they are self-limited; tuberculous pleurisies frequently recover, especially when there is a good eosinophilia; the persistent high temperatures with little remission, with night sweats, and general malaise, suggest a cold abscess which will never be overcome so long as the pleural cavity is a box-like structure. These septic pleurisies can only be overcome by a thoracoplasty.

A pneumolysis may suffice for simply an uncompressed portion of the lung. A cavity held out by adhesions may be thus collapsed; it is possible that a compression of the whole lung may not be needed in order to obtain the obliteration of a circumscribed cavity; when an artificial pneumothorax fails it is quite clearly indicated that the uncompressed upper lobe shall be freed by pneumolysis and compressed. If there is a pleural effusion there is danger of empyema. Cold abscess of the pleural cavity does not seem to be within the reach of a pneumolysis, but Sauerbruch has obtained good results by his method of thoracoplasty. Our five years'

experience of artificial pneumothorax has taught us to question the advisability of allowing patients to go as far as possible before operative interference; it would seem to be a mistake; to prove the best time for undertaking an artificial pneumothorax, some large municipal sanatorium should undertake the study of early cases and report.

We have learned how to induce recovery when there are no complications; to advance the treatment of pulmonary tuberculosis we must go a step farther and learn how to overcome the complications. This demands the coöperation of the surgeon. Surgeons that are distinguished for ability are not familiar with tuberculous conditions or problems. They see the situation entirely from a surgical and not from a tuberculous stand-point; even the most distinguished surgeons enter a *terra nuova* when they begin this work. We need a large sanatorium with an abundance of clinical material, in good surroundings and accessible to the best surgeons, in order that these problems may be worked out for us in the United States as they are being studied in Zurich by Sauerbruch. Our work is behind our needs for lack of sufficient coöperation between the tuberculosis specialist and surgeons of distinguished ability interested in the solving of these problems. There should be a surgical clinic in our large municipal institutions, because these can furnish enough clinical material to give the surgeon sufficient experience. We need a large number of consecutive operations to give us logical inferences. Cincinnati seems ideally situated in this respect. Its municipal sanatorium for tuberculous patients is easily within the reach of the able city surgeons, and its location high upon its breezy hills, affords salubrious surroundings not often found in a city within a short drive. The advancement of our ability to cure tuberculous patients depends upon the surgeons who will take this work up.

## AN UNUSUAL MODE OF RUPTURE OF ANEURYSM, EXPLAINED BY DISCOVERY OF ITS DISSECTING NATURE.

BY FRED. D. WEIDMAN, M.D.

(From McManes Laboratory of Pathology, University of Pennsylvania, Philadelphia.)

THE subject matter of this communication was furnished by an autopsy upon a sailor dying of intracranial hemorrhage from rupture of a saccular aneurysm of the right vertebral artery. The case has been reported from a clinical and morbid anatomical standpoint in another place.<sup>1</sup>

<sup>1</sup> Jour. Am. Med. Assn., 1915, lxy, 1105.

The lesion was of about the size of a pea and lay on the right basilar artery in a large fresh clot. This concealed the aneurysm during the process of severing the cord, during which procedure the aneurysm was either cut or torn in half transversely. Through good fortune the fracture occurred directly at the point of rupture, as was suspected by gross and later confirmed by minute examination.

Grossly it disclosed nothing of its dissecting nature. Its walls were very thin and showed no peripheral fibrosis or adhesions. It contained a small excentric core of fresh clot close to the point of rupture (on the ventral or inferior side) and slightly older peripheral clot with poorly indicated lamination on the opposite side (toward the bulb).



FIG. 1. Transverse section of entire aneurysm at point of rupture. Magnification ca. 8 diameters. The brackets enclose the vital course of the artery wall. The rest is the aneurysmal sac; *bd*, blood dissection between media and adventitia (cf. with Fig. 2), indicated here by a broad pale channel; *l*, lumen of artery.

Microscopic sections were cut from the lower half of the aneurysm, parallel to the plane of fracture, and therefore in the transverse plane of the aneurysm, the small size of which afforded the unusual opportunity of making histological sections of a whole aneurysm, while good fortune placed the sections at the point of rupture.

The histological report follows: On one side the muscular coat is recognizable as such, vital and divided into three segments by blood extravasations and by a gap. On the other side the wall is

highly attenuated, markedly bulged outward, and encloses a thrombus. The latter does not completely fill the vessel, a broad lumen persisting close to the vital side and communicating with the exterior of the vessel by means of the gap mentioned above. The attenuated (aneurysmal) side of the vessel constitutes fully four-fifths of the circumference. Here the different coats are fused, not recognizable as individuals, hyaline, necrotic, but nowhere ruptured. There are no attempts at organization of the overlying thrombus, which is of very recent type. In the periphery of the thrombus the outlines of the red-blood cells are more or less

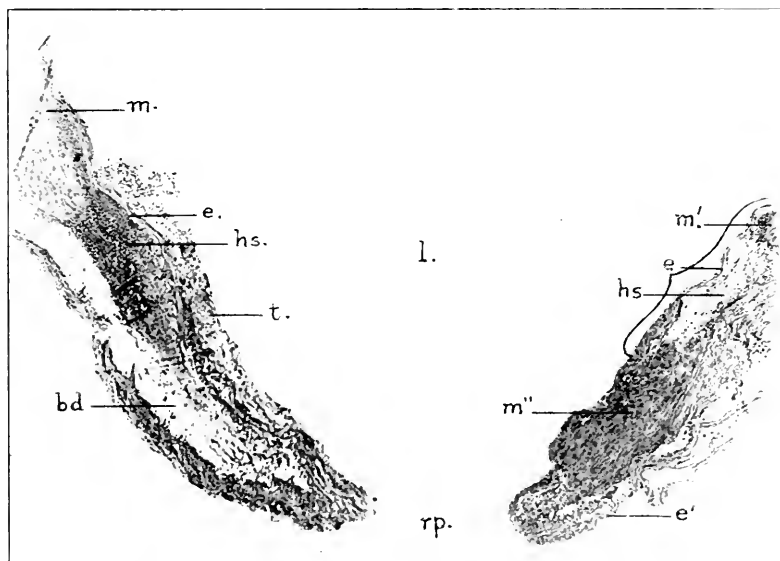


FIG. 2.—Microscopic section showing the artery wall at point of rupture more highly magnified. ca. 50 diameters. *rp*, point of rupture (the “gap” of the text); *m, m', m''*, segmented media; *hs*, intersegmental hiatuses containing blood; *e*, internal elastic lamina. It is continued at *e'* through the gap to the outside of the vessel; *t*, slight thrombosis; *bd*, blood dissection (cf. Fig. 1); *l*, lumen of artery. The bracket indicates the position from which a part of Fig. 3 was taken.

preserved and the leukocytes in fairly vital condition, while the luminal part is very recent, showing fibrin reticulum and cellular elements in excellent condition. The point where the dilatation begins is sharply indicated, and here, on either side, the thrombus extends between and separates the media and adventitia, continuing on one side as a narrow zone quite as far as the gap. On the vital side the media is divided into three segments by hemorrhages which show laked red-blood cells and hemosiderin granules. Over the segments the elastica is corrugated, over the defects serpentine or straight, save at the gap, where it is broken. This gap is directly opposite the aneurysmal dilatation. The intima immediately

adjacent is cloddy, granular, and discontinuous, underlaid by laked red-blood cells and no media. It is overlaid by a thin layer of ropy, hyaline, necrotic material suggesting old thrombus. There is no histological evidence of specific causation.

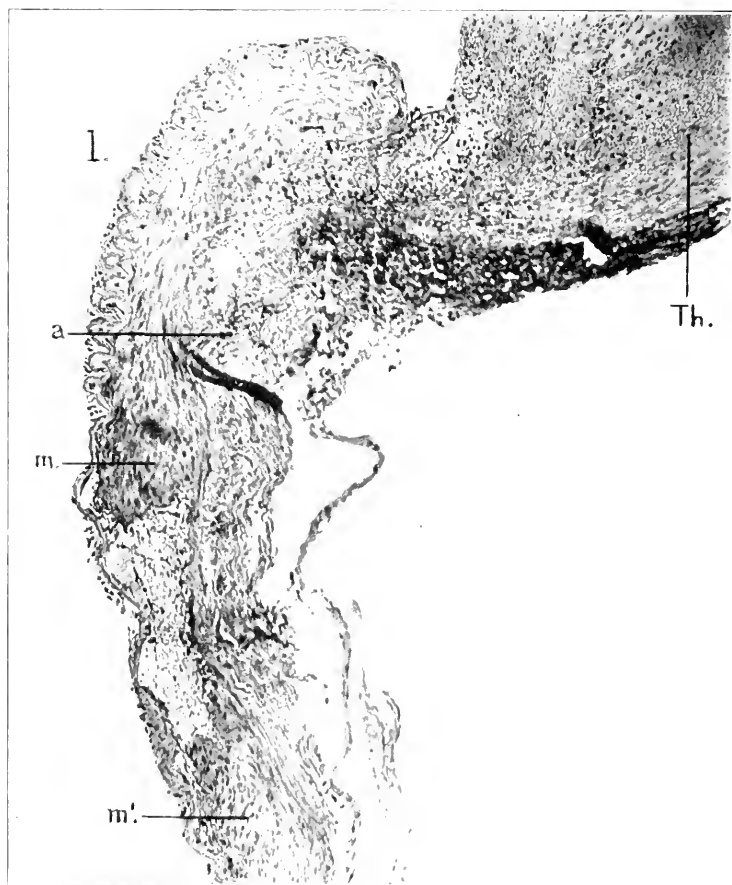


FIG. 3.—Portion of vital part of artery wall near point of rupture (cf. Fig. 2 for location of part and Fig. 1 for relation to whole aneurysm). Magnification ca. 80 diameters. Note corrugated elastica over intact media and stretched elastica over the hiatuses. *Th.*, thrombus in aneurysmal sac extending at *a* between media and adventitia; *l*, lumen of artery; *m, m'*, segments of media; *h*, intersegmented hiatuses containing blood.

Disregarding gross dissecting aneurysms we find that in practically all saccular aneurysms which rupture the point of such rupture is in some part of the aneurysmal dilatation. Theoretically this is the part which should be weakest, and here we expect, and generally find, the point of rupture if rupture has occurred. In the case here reported we find an exception, the rupture taking place not in

the (apparently) weakest part but through the more vital course of the artery wall.

Study of the microscopic section reveals a probable mechanism, showing that the aneurysm is a dissecting one even though the dissecting features be of but microscopic proportions and extent. Beginning at the thrombus in the aneurysmal sac the hemorrhage may be traced on either side, passing circumferentially (circumferentially in the section—it of course extends longitudinally also in the lesion) between the media and adventitia. This means that blood (and pressure) lay in this position, a pressure which was not a constant one, any more than that in the arterial lumen was, and varying, as there, with systole and diastole. However, on account of the more restricted entrance of blood to this position (it had to pass through crevices) the pressure here was probably not quite equal to, nor the systolic and diastolic variations synchronous with, the luminal pressure. These unequal and irregularly timed forces acting on two opposite sides of a media which is normally accustomed to rhythmical influences are probably responsible for its segmentation, and blood would at once enter the hiatuses, as seen in the sections. After this the internal elastic lamina would be abnormally stretched over the intermuscular hiatuses, lose its capacity to assume a corrugated character during diastole and even be forced outward over the hiatuses during systole. This stretching of the elastica ultimately produced degeneration with consequent roughening and thrombus formation such as is noted close to the gap (Fig. 2). When sufficiently weakened, and unsupported by media, rupture must take place, the adventitia alone remaining to withstand the internal blood-pressure, and shortly also rupturing.

The unusual position of the point of rupture, then, is largely explained by dissective features. This said, it must be acknowledged that the small size of the artery was also contributory. It is most likely that so far as absolute distance is concerned, dissection takes place as extensively in aneurysms of large arteries as in this one. But here, on account of the small size of the vessel, this comparatively short distance sufficed to involve its whole circumference; and on account of the normal thinness of its walls, their coats were separated proportionately greater distances. The degree of disorganization and weakening, then, was much greater in this vessel than would have been the case in an aortic aneurysm, the extent of dissection being the same. The support afforded by the medulla probably prevented an earlier rupture of the major aneurysmal sac.

Against this mechanism it might be objected that the intramural blood appears here as the result of dissection in the opposite direction, *i. e.*, from the point of rupture (not from the major aneurysmal sac), occurring several days prior to death, perhaps from a second miliary aneurysm. That a miliary aneurysm of very short duration

was present, due to the dissecting process, may be admitted. That such occurred as part of the same general influences which produced the major aneurysm cannot be conceded, for we note that only unimportant thrombotic features appear at the gap. With aneurysm there should be notable ones. The internal elastic membrane, too, is degenerated only along a small part of its course, practically only at one point. In aneurysm it should show more diffuse degeneration. And, what is of most importance, the media nearby is not degenerated. It is broken and the point of rupture is a point, not a region. Or it might be objected that the intramural blood entered passively when the aneurysm was severed at autopsy. Against this the histological description makes note of retrogressive changes in the intramural blood (pigment and slight hemolysis), indicating that the blood here is not fresh. It is of some standing.

In conclusion the unusual point of rupture in this case was due to:

1. Support of the wall of the major aneurysmal sac by the medulla.
2. Blood dissection from the aneurysm between the adventitia and media of the non-aneurysmal part of the arterial wall.
3. The normal thinness of this artery wall.
4. Lack of support ventrally, the arterial wall abutting directly upon a serous space.

## CALCIUM AND BENCE-JONES PROTEIN EXCRETION IN MULTIPLE MYELOMA.

BY N. R. BLATHERWICK, PH.D.,

NEW YORK.

(From the Chemical Laboratory of the Montefiore Home and Hospital for Chronic Invalids, New York.)

SINCE Bence-Jones, in 1847, first observed the presence of a peculiar protein body in the urine of a patient suffering with bone disease, considerable study has been devoted to this subject.<sup>1</sup> Several have investigated the chemical properties of the Bence-Jones protein, but the factors controlling its excretion remain but little understood. Though the present investigation deals primarily with the calcium metabolism of a case of typical multiple myeloma, the output of the Bence-Jones protein has also been followed.

EXPERIMENTAL. The experiment was divided into three intervals, the first of six and the others of three days each. The diet of high protein content was kept as uniform as possible. The patient, who occupied a special room during the experiment, was under continual observation by day and night nurses. The food

<sup>1</sup> Trans. Roy. Soc. London, 1848, i, 55.



was weighed and prepared in a metabolic diet kitchen. The calcium values of the constituents of the diet were calculated from the tables of Sherman.<sup>2</sup> Urines were placed in a refrigerator until the completion of the twenty-four-hour period. Feces, separated by carmin, were dried to constant weight before analyzing. McCrudden's method<sup>3</sup> was used for calcium determinations, that of Folin and Denis<sup>4</sup> for Bence-Jones protein.

**RESULTS.** In the preliminary period the urinary values for CaO are seen to vary from 0.41 gm. to 0.96 gm., with an average excretion of 0.86 gm. per day; 1.5 gms. were taken in the food while 1.6 gms. were excreted, giving a daily negative balance of 0.1 gm.

Calcium lactate equivalent to 1.18 gms. CaO was administered by mouth each day of the second period. A higher average excretion of urinary calcium (0.84 gm. CaO) resulted. The average daily amount of CaO determined in the feces was 2.67 gms. The balance of CaO with an excretion of 3.51 gms. and an intake of 2.67 gms. was negative, showing a loss of 0.84 gm. daily. Determinations of CaO in the feces of third period could not be made, as bismuth which interfered with the calcium estimations was administered to the patient through an oversight.

The excretion of the Bence-Jones protein was found to be very variable, extremes ranging from 7 to 27.56 gms. Average values for the three periods, 18.56, 17.35, and 19.24 gms. were, however, quite uniform. An increased daily excretion of 2.88 gms. nitrogen in the feces of the second period, followed by 1.81 gms. in the third, may be due to disturbances of absorption, as shown by the development of diarrhea in period II.

**DISCUSSION.** The plane of calcium metabolism was found to be on a high level. With a daily intake of 1.5 gms. CaO an approximate calcium equilibrium was reached. The diet was purposely chosen with a high content of calcium, as analyses of urine and feces made three months previously had shown an abnormally increased excretion of this element. At that time the patient on his fourth day of uniform diet (1.07 gms. CaO) excreted calcium corresponding to 1.04 gms. CaO in the urine and 1.14 gms. in the feces, therefore failing to retain 1.11 gms. daily. The urinary nitrogen elimination was 16 gms.

In the present experiment, when 1.18 gms. CaO in the form of calcium lactate were added to the daily food, there resulted a loss of 0.84 gm. CaO to the body. Thirty-six per cent. of the calcium oxide administered was utilized, as calculated from the balances of the first and second periods. There was an average daily increase of about 0.1 gm. calcium estimated as oxide in the urine over period

<sup>2</sup> Chemistry of Food and Nutrition, 1911, Macmillan, New York.

<sup>3</sup> Jour. Biol. Chem., 1911-12, x, 187.

<sup>4</sup> Ibid., 1914, xviii, 277.

I, but by far the greater part was eliminated in the feces, which could be expected.

As far as the author has been able to determine, calcium analyses in the excretions of multiple myeloma patients have hitherto been undertaken but twice only. In one instance Seegelman found values which varied inconsiderably from the normal.<sup>5</sup> Williams on two days found 0.92 gm. and 1 gm. calcium, calculated as oxide, in the urine of his patient.<sup>6</sup> The latter undoubtedly represent high values.

The daily amount of this element required by a normal man is placed by Albu and Neuberg at 1 gm. to 1.5 gms. CaO.<sup>7</sup> There are examples on record, however, in which calcium equilibrium was attained on a much lower level, 0.4 gm. CaO daily (Bertram). The per diem elimination in the urine is normally between 0.1 and 0.5 gm., calculated as oxide. Our results, as well as those of Williams, greatly exceed the higher of these normal limits. We were unable to secure a positive calcium balance even when 1.5 gms. CaO was administered. This indicates that the calcium metabolism in our patient was operating at a higher plane than normal. That absorption of calcium was active is shown by the partial retention of added calcium in the form of calcium lactate. *These results justify the view that as a result of the osseous lesions a liberation of calcium has taken place which is shown by an increased excretion.*

Bender found deposits of calcium in the lung of a case of multiple myeloma which came to autopsy.<sup>8</sup> In a second case this investigator reported an increased calcium content of the lungs, lymph glands kidneys, gastric mucosa, and liver. The deposits occurred chiefly in connective tissues. Some years later Tschistovitch and Kolesnikowa<sup>9</sup> reported a very noticeable increase in the calcium content of the lungs, while smaller amounts of this element were found in the stomach, kidneys, and intestines. These data make it probable that the disease of multiple myeloma, with its attendant destruction of the bony structures, leads to a liberation of calcium which is chiefly excreted, but which in part may be abnormally deposited in certain organs.

The origin of the Bence-Jones protein has always remained a matter of conjecture. Voit and Salvendi inclined to the belief that *less* of the protein *was excreted* on a protein sparing diet.<sup>10</sup> Allard and Weber, who made the first protein metabolism studies in regard to this problem, found no relationship between the amounts of protein catabolized and the Bence-Jones protein eliminated.<sup>11</sup>

<sup>5</sup> Deutsch. Arch. f. klin. Med., 1897, lviii, 276, 286.

<sup>6</sup> Biochem. Jour., 1910-1911, v, 225.

<sup>7</sup> For a discussion of calcium metabolism, see Albu-Neuberg: Physiologie und Pathologie des Mineralstoffwechsels, Berlin, 1906, p. 111.

<sup>8</sup> Deutsch. Ztschr. f. Chir., 1902, lxiii, 370.

<sup>9</sup> Virchows Arch., cxvii, 112.

<sup>10</sup> München. med. Wchnschr., 1901, li, 1281.

<sup>11</sup> Deutsch. med. Wchnschr., 1906, xxxii, 1251.

Later, Hopkins and Savory, who carried out very careful metabolic studies on three cases of multiple myeloma, came to the same conclusion.<sup>12</sup> Recently, Folin and Denis decided from a study of their case that "there is nothing like a definite or constant relationship between the total nitrogen and the albumose of the urine."<sup>13</sup> The results of our experiments also show a great variation in the amount of Bence-Jones protein eliminated, with no obvious relationship to the nitrogen excretion.

#### PROTOCOL I.—URINARY EXAMINATION.

Day.	Volume, c.c.	Nitrogen, gm.	Bence-Jones Protein, gm.	CaO, gm.
1 . . . . .	1030	13.99	.....	0.4128
2 . . . . .	805	13.15	8.05	0.7511
3 . . . . .	915	13.27	13.73	0.9516
5 <sup>14</sup> . . . . .	1590	17.09	24.91	0.9596
6 . . . . .	945	10.68	27.56	0.6067
7 . . . . .	1030	12.08	19.31	0.8127
8 . . . . .	860	13.00	18.71	0.9761
9 . . . . .	780	10.96	14.04	0.7215
10 . . . . .	1400	13.90	7.00	0.7910
11 . . . . .	1350	11.62	25.70	0.5611
12 . . . . .	1270	13.25	25.02	0.7328

#### PROTOCOL II.—DAILY AVERAGES OF EXPERIMENTAL PERIODS.

Period.	Urine.			Feces.		CaO balance.		
	Nitro- gen.	Bence- Jones protein.	CaO.	Nitro- gen.	CaO.	Ingested.	Excreted	Differ- ence.
I.	gm. 13.64	gm. 18.56	gm. 0.7364	gm. 0.94	gm. 0.8604	gm. 1.5034	gm. 1.5968	gm. 0.0934
II.	12.01	17.35	0.8368	2.88	2.6745	2.6682	3.5113	0.8431
III.	12.92	19.24	0.6959	1.81				

6 gm. calcium  
lactate = 1.1766  
gm. CaO daily  
per os.

ABSTRACT OF CLINICAL HISTORY. I. G., male, aged forty-three years, expressman.

*Family History.* Negative. Typhoid at twelve years; no other previous disease. Admitted January 19, 1915; died July 3, 1915.

*Present Illness* commenced two years previous to admission. Persistent pains in chest, back, groins, and thigh; weakness and diarrhea.

<sup>12</sup> Jour. Physiol., 1911, xlii, 189.

<sup>13</sup> Loc. cit.

<sup>14</sup> Part of the urine was lost on the fourth day. It was accordingly not examined. The specific gravity of the urine was normal throughout.

*Examination.* Thorax shaped like a toad's body, this condition probably resulting from posture and gravity. Exquisite tenderness over the ribs, pelvis, and long bones. No distinct evidence of other organic disease except a diffuse infiltration of the lungs. Roentgen-ray plates showed advanced bone absorption of general nature, including metacarpals and phalanges and a diffuse infiltration (calcium salts?) in the lungs. Blood count: red-blood cells, 3,680,000; white-blood cells, 9000; lymphocytes, 56 per cent.

Deformities of chest increased and severe pains continued until death from pulmonary edema intervened. Diagnosis: multiple myeloma. No autopsy could be performed.

ERRATUM: The diagram which appeared in the article entitled "Some Aspects of the Clinical Study of the Respiration: The Significance of Alveolar Air Analyses," published in this JOURNAL, February, 1916, p. 188, should be corrected so as to correspond to the new diagram herewith shown.



FIG. 1



FIG. 2

## REVIEWS

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DISEASES OF THE DIGESTIVE ORGANS. WITH SPECIAL REFERENCE TO THEIR DIAGNOSIS AND TREATMENT. BY CHARLES D. AARON, ScD., M.D., Professor of Gastro-enterology in the Detroit College of Medicine and Surgery; Consulting Gastro-enterologist to Harper Hospital. Pp. 790; 154 engravings; 48 roentgenograms; 8 colored plates. Philadelphia and New York: Lea & Febiger, 1915.

WITHIN recent years an increasing number of books have been written on the gastro-intestinal tract. Many of them have justified their production while others have seemed somewhat superfluous. In the volume under consideration the author has handled a vast amount of material in such a way as to present the subject matter with great clearness. He has not by any means exhausted his field, but that would be impossible, within the limited scope of such a work. Many notable achievements have recently crowded in upon this branch of medicine covered by Dr. Aaron. Modern research; improved facilities for observation; the development of roentgenographic technic and the perfection of the various tests and reactions have added immensely to possibilities in these lines.

The various chapters are arranged so as to accord with the physiological path of the digestive tract; beginning with oral diseases and proceeding to a consideration of those of the pharynx, esophagus, stomach, liver, gall-bladder, bile ducts, pancreas, small intestines, appendix, colon, sigmoid flexure, rectum, and anus. Throughout these chapters the author must be congratulated upon his endeavor to emphasize the intimate relationship that exists between gastro-enterology and all branches of internal medicine. The author's viewpoint is distinctly that of the internist, although due consideration is given to indications for surgical intervention. In appropriate parts of the book are to be found discussions on the subject of internal secretions; various tests and reactions; qualitative and quantitative analyses for disclosing the condition of intestinal functions; a noteworthy chapter on the examination of the feces; test-meal technic and findings; dietetics; a most valuable chapter on mineral-water therapy; hydrotherapy; mechanical therapeutic agencies; oral sepsis; duodenal feeding and very useful chapters on diseases of the liver and pancreas. A chapter of twenty-six

pages is devoted to roentgenography of the esophagus, stomach, and intestines. Included in this chapter are eleven excellent plates illustrating the various pathological possibilities in the gastrointestinal tract. The Roentgen ray undoubtedly revolutionized the work of the gastro-enterologist and has brought an element of exactness into his diagnoses which often makes an exploratory laparotomy unnecessary.

One of the tests of any work is the realization or non-realization of the author's aim as set forth in the preface. The author, as he proposed to do, "has put before the practitioner in an orderly, consecutive manner the diagnosis and treatment of digestive diseases" and has made "available all the resources of this branch of medicine."

The book is well constructed; the illustrations are adequate and clear cut. The author and publishers are to be congratulated on a book that should be a splendid working manual for the student and an excellent reference volume for the practitioner.

T. G. S.

**MATERIA MEDICA AND THERAPEUTICS. A TEXT-BOOK FOR NURSES.**

By LINETTE A. PARKER, B.Sc., R. N., Instructor in Nursing and Health, Teachers' College, Columbia University. Pp. 311; 29 illustrations; 3 plates. Philadelphia and New York: Lea & Febiger, 1915.

THE amount of knowledge pertaining to materia medica essential for most efficient nursing is always a debated point. There are those who insist that we are overeducating nurses in this respect and again there are others who feel that there can be no limit to the things we teach those who care for the sick. To either of these, this excellently constructed volume can offer no offense, for it appears to be a happy medium in this respect.

In the preliminary sections, tables, technic, and necessary definitions are clearly stated and explained. The consideration of drugs is arranged by systems; nervous, muscular, circulatory, etc., with an additional section devoted to specifics and drugs which affect nutrition. An excellent chapter on legislation, concerning poisons and habit-forming drugs includes a consideration of the Harrison Drug Act and indicates just what drugs are restricted and how to conform to the law. Chapters dealing with psycho, hydro, electro, serum, and ray therapy are well done and give the reader an accurate idea of these useful adjuncts in the treatment of diseases.

The author has an interesting style and a faculty for clear expression. Only the essentials are presented. Emphasis is not placed upon the fact that a certain drug is prescribed in a certain condi-

tion, but upon what action the drug may be expected to have and what untoward effects may be looked for and the emergency procedure pending the physician's arrival in case of an overdose.

The nurse in training who carefully studies this volume and is permitted to have it supplemented by class-room demonstrations of the appearance and characteristics of drugs along the line indicated by the author will bring to the performance of her duties just that degree of knowledge that is most likely to serve the needs of the physician in attendance and the best interests of the patient.

It is seldom that we can commend a work as heartily as we do this one. The engravings are excellent. The volume is well and carefully indexed.

T. G. S.

A TEXT-BOOK OF THE DISEASES OF THE NOSE AND THROAT. By JONATHAN WRIGHT, M.D., Director of the Department of the Laboratories, New York Post-Graduate Medical School and Hospital, and HARMON SMITH, M.D., Surgeon to the Throat Department of the Manhattan Eye, Ear, Nose, and Throat Hospital; Clinical Professor of Laryngology and Rhinology, Cornell University Medical School. 373 illustrations; plates 14. Philadelphia and New York: Lea & Febiger.

THIS product of the brains and life-work of Jonathan Wright and Harmon Smith impresses the reviewer as being the best work on the subject that America has produced. And this for several reasons: In the first place there is present a wealth of real pathology—pathology that is authoritative, first-hand, and thoroughly digested. This portion of the book could be lifted out and published separately as a splendid epitome of the pathology of the diseases of the upper air passages. In the second place, etiology and therapeutics are correlated with the pathology to a unique and most refreshing degree. And finally, there is running through the entire volume an attractive and very obvious and insistent philosophical note—a note which lifts this book to a plane a bit higher than any publication along similar lines with which the reviewer is familiar. With all of this there is no loss of or neglect of the practical side: no helpful little detail which has occurred to the authors being omitted, no matter how trivial.

Much to be commended is the omission of a section on diseases of the ear. Seldom, if ever, does a single text-book deal with both the nose and throat and the ear and do justice to both. One unpleasant result always follows, and that is a volume of unwieldy size. The day soon should come when, on account of the size of the subject, good text-books on the entire field of rhinology and laryngology can not be written. This tendency is plainly manifest

now, when volumes are being issued on such subtopics as bronchoscopy, the sinuses, the tonsils, etc. But in spite of the increasing breadth of the subject, Jonathan Wright and Harmon Smith have given us a book which covers the entire field, yet withal in so concise a manner as to make a volume of handy size, and yet in so direct and complete a fashion as to be of great help to the mature specialist and a veritable *cade mecum* to the general practitioner and to the beginner in laryngology and rhinology.

The book is well printed, well illustrated, and well indexed. Errata there are and omissions there are, as in all books of this character, but these do not alter the general proposition that rhinological literature has received a valuable addition: valuable not only because it is a unique and authoritative combination of the clinical and pathological, but also on account of the rare philosophical tone which characterizes it throughout. G. F.

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MEDICAL AND SANITARY INSPECTION OF SCHOOLS. By S. W. NEWMAYER, A.B., M.D., in charge of Division of Child Hygiene, Bureau of Health, Philadelphia. Pp. 311; 85 illustrations. Philadelphia and New York: Lea & Febiger.

THIS is a good book, and comprehensively written by one evidently familiar with the subject. The reading matter is divided into four parts: administration; school buildings and grounds; infectious, contagious, and communicable diseases; physical defects.

The section on administration includes the organization of bureaus of child hygiene, the duties of the medical inspector and nurse, and various systems of medical inspection. The descriptive plan is comprehensive, and no one can read it without a very good working knowledge of medical inspection. The official statistics taken from the New York reports are good, but those from Philadelphia unfortunately are rather limited and obsolete, being for the year 1910. The medical provisions of the new Pennsylvania School Code are, however, given fully, and serve well as a model for action in other States.

The section on school grounds and buildings is well written, containing the report of the Committee of Medical Inspection of Schools of the American Medical Association, excerpts from the Pennsylvania School Code covering the subject matter of school sanitation, and the Massachusetts Act restricting the use of common drinking cups. School furniture and ventilation are intelligently discussed.

The section on infectious and communicable diseases gives the ordinary methods of transmission of contagious diseases, adminis-



trative considerations in the schools, including the exclusion of children and the quarantine periods. The publishers have furnished most excellent colored plates of vaccination pustules, sore throats of different types (follicular tonsillitis and diphtheria), and Koplik spots in measles.

The section on physical defects includes the consideration of the eyes, ears, nose, and throat, orthopedic defects, systemic diseases, and mentality. These subjects are all well treated, much better than in the average book. The chapter on the teeth is particularly good. The illustration showing objects as they appear to a child suffering from astigmatism produced by the insertion of a cylindrical lens before the camera is hardly true to nature, as it takes no account of that improvement in the sight of such individuals which results from the repeated changing of the focus and from differences which frequently exist in the axis of astigmatism of the two eyes.

The subject of mentality is very fairly written, the usual causes of mental retardation being stated, and also the Binet-Simon tests given are fully reported. This chapter, however, is not quite up to the general standard of the book, the term "feeble-minded" being used exclusive of imbeciles and idiots, and no distinction being made between the feeble-minded who are degenerate and those who are in such condition from accidental brain injuries. In justice to this chapter it should be said that it does present the matter to a non-expert reader in such a way that familiarity and confidence are obtained.

The book closes with the citation of questions asked in civil service and other competitive examinations for the position of school medical inspector, valuable to physicians considering entrance into public health work.

W. S. C.

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CANCER: ITS STUDY AND PREVENTION. By HOWARD CANNING TAYLOR, M.D., Gynecologist to the Roosevelt Hospital, N. Y.; Professor of Clinical Gynecology, Columbia University. Pp. vi, 331. Philadelphia: Lea & Febiger.

THE author aims to give the practitioner a summary of the most important facts now at hand concerning malignant neoplasms, to place such knowledge as is of practical value in the handling of these cases in an easily accessible form, and to point out how important it is that greater care be taken by the practitioner in collecting accurate statistics upon the cancer problem in order to further our knowledge of the subject.

The first third of the book is devoted to the etiological factors apparently influencing the development of cancer, to the statistical

evidence of its increasing frequency, to theories of its nature, and to a discussion of its contagiousness and of the nature of metastasis, recurrence, and cachexia. The subject is treated from the clinical aspect with only occasional references to the recent experimental work. This is no doubt because the experimental work has not yet reached a stage which permits of many deductions of practical importance to be drawn from it. On the other hand, barring this experimental work, little that is new has been added to the general problem of the malignant neoplasm in recent years, so that this portion of the work is for the most part a restatement of the views that have prevailed for many years. The latter two-thirds of the book is devoted to a systematic presentation of the etiology, pathology, symptomatology, diagnosis, and treatment of carcinoma and sarcoma of the various organs of the body—being a considerably fuller account of this portion of the subject than is given in the general text-book of medicine, and being thoroughly up-to-date.

J. H. A.

THE MEDICAL CLINICS OF CHICAGO. By VARIOUS CONTRIBUTORS. Vol. I, Nos. 1, 2 and 3. Pp. 605. Philadelphia and London: W. B. Saunders Company, 1915.

THE *Medical Clinics of Chicago* have manifestly been brought out for the purpose of occupying in the medical world a position similar to that which is held by Murphy's *Clinics* in the surgical field. They follow the same general plan as do their surgical predecessor and in many ways are entirely similar. They lack, however, one of the strongest appeals of Murphy's *Clinics*, the dominant personal touch of a strong and brilliant man whose personality pervades each page. This is not said with any idea of disparaging the several contributors to the *Medical Clinics*, for it is obvious that among ten contributors some of their presentations would be lacking in something and would fall behind the others in general merit, thus weakening the general value of the whole work.

The plan of the clinics is to present a case, as in any clinic, to demonstrate it, and from this case to draw conclusions and likewise to use it as a text for a general discussion of the particular disease from which the patient is suffering. Ordinary clinics are of undoubted worth; they impress the hearers through their sense of sight and of hearing. Clinics presented in writing lack that appeal to the eye and ear which makes a clinic of value. They have all the faults of an ordinary clinic without the attending circumstances which mitigate the shortcomings of the clinic that is heard and seen. Likewise a carefully prepared paper written with thought and consideration,

without irrelevant interruptions, can be read with far greater value by the physician than a stenographical report of what a man has spoken extemporaneously. If then such articles lack the appealing elements of a seen clinic and the knowledge to be derived from the perusal of a scientific paper, in what does their value consist? The answer to this question is that this work will be bought and read by the man who does not care to read scientific papers, by the man who has not the opportunity of seeing clinics, by the man who likes discussions of every-day problems, and by the man who is so tired after a hard day's work that he is unable to follow the conventional medical publications with any degree of concentration. To such men the medical clinics will have a very real value.

The contributors to the past three numbers of these clinics include Drs. I. A. Abt, M. L. Goodkind, W. W. Hamburger, R. C. Hamill, C. L. Mix, R. B. Preble, W. A. Pusey, F. Tice, R. J. Twosen, and C. S. Williamson.

If it is conceded that such a work has a certain place to fill in medical writings, a better list of contributors would be difficult to secure in Chicago or in fact in any large city. J. H. M., Jr.

A GUIDE TO THE USE OF TUBERCULIN. By ARCHER W. R. COCHRANE, M.B. (Lond.), F.R.C.S. (Eng.), Major in Indian Medical Service; Medical Superintendent, King Edward VII Memorial Sanatorium, Bhowali, United Provinces; and CUTHBERT A. SPRAWSON, M.D., B.S. (Lond.), M.R.C.P., Major in Indian Medical Service, Professor of Medicine, King George's Medical College, Lucknow; Physician to King George's Hospital and to the Lucknow Tuberculosis Hospital. Pp. 181; 84 charts. New York: William Wood & Co., 1915.

THIS book is an attempt on the part of two men who have had a large experience in the use of tuberculin to reduce to writing the general rules which have guided them. They regard fully 75 per cent. of the cases of pulmonary tuberculosis coming to them as suitable for tuberculin treatment, and they do not consider a secondary infection by other organisms or a hemoptysis as a contra-indication. They do, however, regard as contra-indications marked emaciation, tuberculous diarrhea, a very rapid pulse, a high and continued fever, and acute disease. Special emphasis is placed upon temperature and weight records as guides to the continuation of treatment, the proper interval between doses, and the proper doses. The charts displayed in the book are numerous and most instructive. Only enough theory is given to make appreciable the clinical and pathological aspects of tuberculin therapy. While

the number of cases which they regard as suitable for tuberculin injections seems large, there is evident a marked conservatism in their method of applying the treatment, and the thought is forced upon us that some of our failures may have been due to faulty application.

T. G. M.

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THE MENTAL HEALTH OF THE SCHOOL CHILD. By J. E. WALLACE WALLIN, PH.D., Director-Elect of the Psycho-Educational Clinic, St. Louis Public Schools. New Haven: Yale University Press.

IN this book the author has endeavored to cover the field of clinical psychology in its modern aspects, correlating it with school medical inspection and the physical health of the child, and to furnish a compendium of information concerning organized activities in this field throughout the United States.

The book contains nineteen chapters which in brief include the consideration of clinical psychology, the functions of the psychological clinic, psychological research among epileptics (in which group Dr. Wallin has had much valuable special experience), the present status of the Binet-Simon tests, and the relation of physical health to mental development, including special consideration of the relation of carious teeth to mental development.

There is also presented a skeleton outline for the recording of case histories when dealing with supposedly deficient children, the field of investigation covering social, medical, psychological, and educational information.

Taken together, the book is full of interesting facts, gathered evidently at great labor and correlated by one with a keen analytical mind. The book is really one of the most valuable contributions of solid material to those interested in mentally deficient children. Extensive bibliographies are given at the end of several of the chapters, and the appendix contains a mass of statistical information concerning the work that is being done by educational authorities in different American cities, the places at which instruction is given in the subjects, and the cities in which special instruction for tuberculous, blind, crippled, etc., children is given.

The most valuable features of the book are the commentaries upon the value and limitations of the Binet-Simon psychological tests, the mental condition of epileptics, and the great mass of information, statistical and otherwise, concerning the education of deficient children throughout the United States.

The only points in the book which may be reviewed in a critical spirit are the chapter on the relation of decayed teeth to the mental development, the repetition of the writer's views upon the limits of the Binet tests, and the tendency to use language which, while

thoroughly sound and scientific, might be replaced by simpler English words.

Regarding the relation between dental caries and mental development the conclusions are possibly premature. In the matter of the limits of the Binet tests the reviewer agrees with the author absolutely in his conclusions, but does not feel that the claims of the ardent advocates of these tests as a diagnostic measure are worth combating so constantly.

Altogether, the book is one that every person giving special study to the subject of mentally deficient children would do well to possess.

W. S. C.

MANUAL OF SURGERY. By ALEXIS THOMSON, F.R.C.S. (Edin.), Professor of Surgery, University of Edinburgh; Surgeon to Edinburgh Royal Infirmary; and ALEXANDER MILES, F.R.C.S. (Edin.), Surgeon to Edinburgh Royal Infirmary. Fifth edition; two volumes. Pp. 1724; 590 illustrations. London: Henry Frowde; Hodder & Stoughton, 1915.

THESE two volumes comprise two-thirds of the work by these authors on surgery. One volume considers general surgical questions, the second takes up regional surgery, and the third treats the operative side of all surgery. In many ways this arrangement is an advantage, making it much handier and convenient in reference.

This, the fifth edition, has improved the entire work. The subject matter on pathology and treatment has been brought up to date. Many new illustrations have been added and all debatable questions left out entirely. The arrangement of the subject matter is very good. The paragraphs on surgical anatomy that frequently head the chapters are a great help and save much time when one is making a detailed study of the subject. The idea is an excellent one and is especially serviceable to students.

The text is remarkably free from useless references and bibliography. No space is given to theorizing. Facts are stated when definitely known. Each subject is treated in its entirety, *i. e.*, its etiology, symptomatology, complications, diagnosis, and treatment.

The style of the text is very pleasing, the expression to the point, clear, concise and smooth. The illustrations are good and really illustrate their subject. In some cases, however, the stage of the disease shown seems a little far advanced. Diagnosis should be made early and illustrations should aid in doing this rather than in showing final stages of disease.

The book itself is well put up. It is handy in size, the print is clean and easily read, and the paper all that could be desired.

The work is a good one.

E. L. E.

**DIFFERENTIAL DIAGNOSIS.** By RICHARD C. CABOT, M.D., Assistant Professor of Clinical Medicine, Harvard University Medical School, Boston, Mass.; Chief of the West Medical Service, Massachusetts General Hospital. Vol. II. Pp. 709; 254 illustrations; 22 charts; one colored plate. Philadelphia and London: W. B. Saunders Company.

THIS new volume of Dr. Cabot's work is modelled along the lines of the well-known earlier volume. The author presents the clinical history, physical examination, and laboratory findings of a series of illustrative cases, discusses the diagnosis on the basis of these data, and then gives either the autopsy findings or the diagnostic evidence from the further course of the case. No more vivid means of presenting bedside diagnosis in book form can be conceived, and the careful study of the material which he presents is exceedingly instructive as well as entertaining. Each of the nineteen chapters is devoted to cases exhibiting some particular symptom or physical finding as follows: abdominal and other tumors, vertigo, diarrhea, dyspepsia, hematemesis, glands, blood in the stools, swelling of the face, hemoptysis, edema of the legs, frequent micturition and polyuria, fainting, hoarseness, pallor, swelling of the arm, delirium, palpitation and arrhythmia, tremor, ascites, and abdominal enlargement. In all 317 cases are detailed. At the beginning of each chapter the author devotes a few pages to a discussion of the general subject of the chapter, and presents in chart form some statistical material concerning the relative frequency with which various conditions give rise to the disorder under consideration. The work is freely illustrated with temperature charts, diagrams of the physical findings, blood charts, etc.

J. H. A.

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**THE GOLD-HEADED CANE.** By WILLIAM MACMICHAEL, M.D., with an introduction by WILLIAM OSLER, B.A., M.D., F.R.S., and a preface by FRANCIS R. PACKARD, M.D. Pp. 254. New York: Paul B. Hoeber, 1915.

THE present edition of the *Gold-headed Cane* is gotten up in an attractive and tasteful manner. The brief biographical sketches of Radcliffe, Mead, Askew, Pitcairn, and Baillie, as presented in this volume, will doubtless be welcomed by all interested in historical medicine.

J. H. M., Jr.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

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**Partial Occlusion in the Treatment of Aneurysms.**—MARTIN (*Surg., Gynec. and Obst.*, 1915, xxi, 629) reports 3 interesting cases of pulsating exophthalmos, due to trauma, and completely cured by ligation of the common carotid artery alone in 1 case and partial ligation of this artery and some orbital veins in 2 cases. The treatment indicated in these cases, due to arteriovenous aneurysm, would be, after preliminary tests as to the effect of compression of the carotid: (1) An occlusion of the vessel by an absorbable ligature up to the point of stopping the bruit and pulsation. The patient can best testify as to the disappearance of the bruit but must distinguish between a true ear tinnitus which often follows basal fracture and the rhythmically throbbing noise of his aneurysm; (2) ligation of one or more dilated orbital vessels; (3) starvation diet, guarding against acidosis, with but little fluid; bowel evacuations, accomplished without straining, and two weeks' rest in bed made, if not alluring, at least bearable by the judicious use of anodynes.

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**Typhoid Perforation.**—GIBBON (*Ann. Surg.*, 1915, lxii, 385 and 539) collected and studied 139 cases from the records of the Pennsylvania Hospital. He believes that our errors result not from any lack of knowledge of symptoms, but rather from a hesitancy to comprehend the importance of promptly acting when these symptoms present themselves. The two most valuable symptoms are pain and rigidity, and on these symptoms we must rely nearly altogether. Of course, if the pain comes on suddenly and the rigidity is marked, a perforation must be suspected and the exploration made. The less sudden and severe the pain and

rigidity, the more difficult the diagnosis becomes. Digital examination per rectum should always be made and often will reveal the very significant acute tenderness. The absence of a leukocytosis is of no diagnostic value. As a rule it takes from eight to twelve hours for the average case of perforation to develop a leukocytosis. The presence of a leukocytosis, of course, is of diagnostic value. There should be no delay in operating if the surgeon believes from the symptoms that a perforation has probably occurred. A quick exploration does not do much damage, but delayed operation is the cause of the high mortality. The safest rule regarding anesthesia, is to open the abdomen under infiltration anesthesia and administer a general anesthetic only if it is necessary, and then for as brief a time as possible. The rule in Gibbon's cases was to close the perforation with drainage of the abdomen but in a number of cases the perforated bowel was sutured in the abdominal wound and allowed to drain. Continuous enteroclysis is the most important part of the after-treatment. The Fowler position, although of great help in many cases of perforative peritonitis, is not always advisable in typhoid fever, as the patient is often too weak to stand it.

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**Fractures of the Femur.**—STEINKE (*Ann. Surg.*, 1915, lxii, 610) says that much has been written concerning the fractures of all bones but the femur presents some of the greatest difficulties to be encountered while its anatomical and physiological importance accentuates the necessity for a good result. Steinke followed up the late results of 62 cases taken from the records of the Episcopal Hospital, 15 of the fractures occurring through the neck of the femur, 6 through the trochanters, 36 through the shaft and 5 through the lower end. As to treatment, the non-operative gave as good results, functionally, as the operative, although the plated cases were selected, which without operation most certainly would have given poor results. Good approximation and alignment of the fragments is not necessary for a straight and unshortened limb. Fractures of the neck were more frequent in the aged of the female sex, indirectly cause a high mortality because of the age of the patient and the lowered resistance, and gave a moderate disability period. Fractures through the trochanters were all in males and gave a long disability period with lowered earning capacity in two-thirds of the cases. Fractures of the lower end of the femur gave an average disability of about six months, while a good functional result was obtained in about one-half of the cases. They were all males. Fractures of the shaft gave the best results and had the shortest disability period. They were the most frequent and were mostly males. The mortality from fractures of the femur other than of the neck was low, being about 2 per cent. in this series.

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**Obturator Hernia.**—McMAHON (*Ann. Surg.*, 1915, lxii, 710) says, quoting Meyer, that the diagnosis at best is only a probable one and that operation should therefore be early. He reports a case operated on in which, although the patient said he had a hernia for four years and gave the signs of having suffered from strangulation for a week, the hernia could not be located until the abdomen had been open. It could not be reduced until after exposure of the hernia in the obturator



region. Recovery was uneventful; the bowel after the reduction of the hernia having no evidence of circulatory impairment. In view of the difficulty of positive diagnosis and the difficulty of exposing the obturator region by dissection, a preliminary median abdominal laparotomy seems a sensible procedure in suspected cases of obturator hernia. It has the following points of advantage: The diagnosis is cleared up at once. The possibility of making an exposure of the obturator region only to find no hernia there is avoided. The abdominal incision greatly facilitates any necessary repair of the herniated intestine. In cases where the condition of the patient demands quick work, the hernia can be reduced from within the abdomen, relieving the constriction under direct inspection with the patient in the Trendelenburg position. The obturator opening could then be closed by a few sutures from within. When the patient's condition permits, the obturator region can be exposed and the sac dissected free and ligated. Inasmuch as it establishes the diagnosis at once and facilitates subsequent operative procedure, preliminary laparotomy seems extremely rational. The modern system of prompt laparotomy in the early stages of all cases of intestinal occlusion will, no doubt, very much lower the mortality-rate in future cases of obturator hernia.

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**The Action of Radium on Transplanted Tumors of Animals.**—WOOD and PRIME (*Ann. Surg.*, 1915, lxii, 751), working under the George Crocker Special Research Fund at Columbia University, used rat and mouse tumors of various types, among them the Ehrlich spindle-cell mouse sarcoma, the Flexner-Jobling rat carcinoma, and mouse carcinomata No. 11 and No. 180 of the Crocker Fund series. These were treated either after removal from the host or *in situ*. In the former method a portion of the tumor to be used was cut into small pieces of uniform size, and these were moistened with Ringer's solution, put into hollow slides, covered with a thin cover-glass, sealed with paraffin, and exposed to the tubes of radium. Their conclusions are as follows: Three factors only are important in the action of radium on tumors: time of exposure, amount of radium element, and distance between the radium tube and the tumor tissue. The removal by suitable filters of the larger part of the beta rays diminishes proportionately the effect of the radium, but the effect of the gamma rays is in accordance with the same general law which governs the beta rays. Sublethal exposures slow the growth of tumor cells for some time, while shorter treatments seem to stimulate the cellular activities. The facts derived from their experiments regarding the quantity of radium element and the time of exposure necessary for a given distance may be applied, with reasonable accuracy, to human malignant tumors. The experiments show also that when only pure gamma rays are used the necessary exposure is eight times as long as that required when the gamma and hard beta rays combined are employed, but as the latter are largely absorbed by 1 cm. of tissue the gamma rays alone must be used for all the deep work. The effect of the radium radiations on tumor cells *in vitro* is less marked than is that on isolated cellular elements. This explains the fact that an exposure which will destroy a small metastatic nodule in man is quite ineffective in the case of a well-vascularized primary carcinoma.

## THERAPEUTICS

UNDER THE CHARGE OF

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**The Effect of Carbon Dioxid in the Inspired Air on Patients with Cardiac Disease.**—PEABODY (*Arch. Int. Med.*, 1915, xvi, 846) describes experiments in which normal individuals and patients with cardiac or cardiorenal disease have been made to breathe air containing increasing amounts of carbon dioxid. The carbon dioxid content of the inspired air was determined for each subject, and the total ventilation of the subject per minute was measured at frequent intervals. Peabody found that normal individuals react to carbon dioxid in a fairly constant manner, and that their total ventilation is doubled when the carbon dioxid content is between 4.2 and 5.4 per cent. of the inspired air. Patients with cardiac and cardiorenal disease well compensated, who are without acidosis as indicated by the carbon dioxid tension of the alveolar air, react in a manner similar to normal subjects. However, patients suffering from these same diseases, but with decompensation and with acidosis are much more susceptible to the carbon dioxid in the inspired air. Dyspnea is more easily produced than in normal subjects or in patients without acidosis and the ventilation may be doubled when the inspired air contains only 2 to 3 per cent. of carbon dioxid. That the increased sensitiveness to carbon dioxid does depend on the acidosis was clearly demonstrated in 2 cases. Peabody says that while acidosis is not the only factor causing the dyspnea in cardiac and cardiorenal disease, it may be an element of considerable importance in producing the clinical picture of decompensation. The article suggests strongly as a therapeutic measure to relieve dyspnea, the correction so far as possible of acidosis occurring in patients suffering from cardiac or cardiorenal disease.

**The Acidosis of Chronic Nephritis.**—PEABODY (*Arch. Int. Med.*, 1915, xvi, 955) says that in mild cases of uncomplicated chronic nephritis, in which the phenolsulphonephthalein test shows a normal renal function there is usually little or no acidosis. More advanced cases, showing moderate or even extreme decrease in the phenolsulphonephthalein output, show an acidosis by the "alkali tolerance" test, but there may be no fall in the alveolar carbon dioxid tension. Only in very advanced cases is the acidosis usually so marked as to cause a decrease in the alveolar carbon dioxid tension. Most cases in which the alveolar carbon dioxid tension is below normal show a phenolsulphonephthalein output which is below 10 per cent. in two hours. On the other hand, cases showing a phenolsulphonephthalein output of "traces" or less may have a normal alveolar carbon dioxid tension. The acidosis of chronic nephritis is due to a retention, resulting from inefficient renal

excretion. Acidosis is probably a very constant feature of uremia, but only in a limited number of cases is it of sufficient grade to cause definite clinical symptoms analogous to those seen in advanced diabetes. In these cases the symptoms caused by the acidosis may be relieved by alkali therapy.

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**The Treatment of Amebic Dysentery.**—Low (*Brit. Med. Jour.*, 1915, 2863, 714) says that emetin may be regarded as a specific drug in the treatment of the amebic form of dysentery and can be given intravenously, subcutaneously, intramuscularly, or orally. Intravenous administration may be adopted in moribund or fulminant cases, but the other methods are preferable for general use. The subcutaneous injections often result in local pains and stiffness which may last for several days, and the same effects may follow intramuscular injections, but are less frequent. Intramuscular injection is the most suitable method of administering emetin, but care should be taken to avoid giving successive doses into the same region. Intramuscular and subcutaneous injections are not followed by nausea or vomiting, even when large doses are given, but these symptoms may result from oral administration. So far as curative effects are concerned, there is no choice of mode of administration so long as the drug is retained. For oral administration the drug should be given in keratin-coated tablets at bedtime. For injection the dose should be two daily injections of a grain each for the first few days, and thereafter one grain every evening until a total of 12 grains have been given. If the symptoms are not all relieved, the disease is probably due to some cause other than the ameba. The action of the drug on the vegetative or living stage of the ameba is very rapid, the parasites quickly disappearing, as do also the blood and mucus and other symptoms. Emetin is said not to effect the ameba in its encysted form, but in the experience of the author daily doses of 1 grain each quickly caused these forms to disappear from the stools. The treatment of the chronic cases and carriers is therefore the same as for the acute cases. Bed treatment is not now necessary, but careful attention to the diet and a systematic course of emetin is essential to a cure. Low notes that the incidence of liver abscess complicating amebic dysentery is much less with emetin treatment.

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**Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis.**—SACHS (*Jour. Amer. Med. Assn.*, 1915, lxy, 1861) reviews critically the results obtained by twenty-four American observers in the treatment of pulmonary tuberculosis with artificial pneumothorax. The author in his conclusions states that experience with artificial pneumothorax in the treatment of pulmonary tuberculosis is gradually modifying the sphere of its application. The trend is toward its use, regardless of stage, in all progressive cases (particularly with unilateral involvement) which fail, after sufficient trial, to respond to strict sanatorium regimen. Complications incident to the employment of this method, the great importance of continuous strict observation and thorough clinical, laboratory and Roentgen study of each individual case, the period essential after each reinflation, the inability of outlining in advance the time of reinflations, in short, the close dependence of each

successive step in pneumothorax therapy on the varying condition of the patient, are all factors which call, in the majority of cases, in the interest of safety and best results, for hospital or sanatorium supervision, at least for a few months, of each individual case in which the method is being applied. Close attention to every important detail of technic, as well as strict asepsis, is also less of a problem, under such conditions, regardless of the excellent results obtained by some observers in dispensary and office practice. The present tendency, grown out of experience, is toward greater conservatism in the selection of cases, a selection based on thorough preliminary study and full consideration of the possible effect of compression in the individual case. Conservatism needs to characterize each successive step in the gradual attainment and subsequent maintenance of a satisfactory compression, with avoidance of too frequent reinflations and excessive intrapleural pressure. This attitude is very important, with a method the application of which cannot be subject to rule, but is dependent on the condition of each individual case. Through improvement of various details of technic and greater conservatism of action, pneumothorax therapy is gradually finding its defined place in the treatment of cases of pulmonary tuberculosis which do not yield to other methods.

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**Observations on Antityphoid Vaccination.**—NICHOLS (*Jour. Exper. Med.*, 1915, xxii, 780) says that the living sensitized typhoid vaccine is not without danger for general use, especially in the military service, as it retains the power of causing typhoid fever if accidentally taken by mouth. He also points out the non-relationship between virulency and toxicity. The army strain, although pathogenic and relatively avirulent nevertheless is distinctly toxic, and it is upon this latter factor that its efficacy depends. In regard to Gay's typhoidin skin reaction, Nichols believes that it is not an index of true immunity, but rather an indication of typhoid protein sensitization, which is not as complete, permanent or specific as true immunity.

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**The Late Results of Active Immunization with Diphtheria Toxin-Antitoxin and with Toxin-Antitoxin Combined with Diphtheria Bacilli.** PARK and ZINGHER (*Jour. Amer. Med. Assn.*, 1915, lxx, 2216) in an earlier report found that the cases injected could be divided into two sharply differentiated groups: (1) Those who had a natural antitoxin immunity produced a very decided increase in the amount of antitoxin after injections of toxin-antitoxin. The response was very prompt and followed even after a single injection. These individuals were, however, naturally immune even before the injections, and needed no further immunizing injections. (2) Those who had no natural antitoxin immunity and were therefore probably susceptible to diphtheria gave entirely different results. An early response (within from four to six weeks after the injections) to the active immunization was noted in only 25 to 30 per cent. of the injected individuals. The examination of the blood serum of these patients for antitoxin showed the presence of from one-tenth unit to ten units per cubic centimeter. Among those who did not definitely respond, however, a number gave a fainter Schick reaction than the control test made before the injections of toxin-antitoxin. This showed that at least a

trace of antitoxin had developed in the cells and had accumulated in the blood. When these individuals were retested from six to eighteen months later, a large proportion now gave a negative Schick reaction and were thus found to have finally become immune. Their results in active immunization up to the present time have led the authors to the conclusion that, while the toxin-antitoxin injections cannot be depended upon to prevent diphtheria in the presence of immediate danger of infection because of the slow development of immunity in a majority of cases, yet the injection is of value in rendering a community or school population immune to the dangers of infection from future exposure up to a period of possibly several years. The authors conclude from their experience with these injections that individuals who, before treatment, give a negative Schick reaction are immune probably for life and, therefore, it is not necessary to inject them, when exposed, either with antitoxin or toxin-antitoxin. Those who give a positive Schick reaction and are exposed to diphtheria and in immediate danger should receive either antitoxin alone or, if a longer protection is desired, both antitoxin and toxin-antitoxin. For the general prophylaxis against diphtheria in schools and communities, excluding immediate contacts, a mixture of toxin-antitoxin alone (from 85 to 90 per cent. of the L+ dose of toxin to each unit of antitoxin) or toxin-antitoxin plus vaccine of killed diphtheria bacilli is recommended. The dose is 1 c.c. of toxin-antitoxin and 1,000,000,000 bacteria injected subcutaneously and repeated three times at intervals of six or seven days. Sufficient time has not as yet elapsed to judge the value of adding the injections of the bacilli to the toxin-antitoxin. The early and the late results of active immunization should be determined with the Schick test. Early results are those obtained by the application of the test within four weeks, and late results from four months to two years after the immunizing injections.

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**The Treatment of Paresis by Injections of Neosalvarsan into the Lateral Ventricle.**—HAMMOND and SHARPE (*Jour. Amer. Med. Assn.*, 1915, lxx, 2147) present a preliminary report dealing with the injection of salvarsanized serum and small doses of neosalvarsan directly into the lateral ventricle for the treatment of general paresis. The report shows that the operation can be successfully performed and they believe that further experience with selected early cases will show a decided superiority to other methods of treatment from a clinical standpoint. The authors state that, in comparison with the deadly nature of paresis, the hazard of intradural treatment, by whatever method, is of little moment. On experimental and clinical grounds both subdural and intraventricular methods are superior to the intraspinal route, in the treatment of paresis. They believe, furthermore, that the intraventricular method is not only superior to the subdural route, but also safer. The intraventricular method, with careful technic, and a due regard for the anatomy of the brain and the delicate nature of the tissues is practically free from danger. The authors are of the opinion that if the freedom from unfavorable symptoms so far achieved in intraventricular injection can be maintained, it will be imperative to so treat paresis in its earliest stages, with greater chance of marked improvement and perhaps permanent arrest of symptoms.

**The Treatment of Syphilis of the Nervous System by Intradural Injections of Salvarsan.**—WILE (*Jour. Lab. and Clin. Med.*, 1915, i, 119) reports fifteen cases of various forms of syphilitic disease of the central nervous system treated by intradural injections of old salvarsan. None have suffered any ill consequences. In all but 2 patients definite objective improvement could be noted in the spinal fluid. With full allowance for the possible suggestive element, there was, nevertheless, a marked subjective improvement in the majority of the cases. Such improvement was not seen to be transitory, but appears to be permanent. Three patients have disappeared from observation, but none of the remaining 12 have relapsed with regard to symptoms. Four patients have been restored to usefulness and are making a livelihood, which before their treatment they were unable to do. The patients showing the most marked improvement were those suffering from early brain or cord syphilis, but encouraging results were also noted in cases of tabes dorsalis. No patient received over three injections, but it seemed to the author that further treatment in cases in which improvement had occurred would be indicated.

**The Reflex Effects of Alcohol on the Circulation.**—LIEB (*Jour. Amer. Med. Assn.*, 1915, lxiv, 898) upon the ground of experimental and clinical observations, says that small doses of undiluted whisky cause a reflex effect on the circulation in a certain percentage of the patients. The reflex is most evident in those cases with hyperactive superficial and deep reflexes, least evident in those who are apathetic as a result of bacterial toxemia. It is more marked in moderate users of alcohol than in those who use alcohol to excess. This is probably due to the protective secretion of mucus which is present in alcoholic gastritis. The reflex is elicited only by irritating concentrations of whisky. Well-diluted whisky causes practically no changes in the circulation before absorption. The degree of response varies more or less directly with the degree of irritation induced; that is, with the dose and the concentration. The changes produced in the heart rate are so small that they are well within the normal fluctuations. The systolic blood-pressure is raised only slightly. The maximum is reached within the first minute, and there the pressure declines so that it reaches normal in less than half an hour. The diastolic pressure is also raised, proportionately less than the systolic, but the return to the original level is very much slower. As a result, the pulse pressure, which was temporarily increased immediately after the whisky was swallowed, is permanently decreased. That is, the pulse after a fleeting increase in size becomes smaller. In some individual cases the decrease in pulse pressure is brought about by a disproportionate rise in the diastolic pressure as well as by its comparatively slower decline. From these investigations it is apparent that alcohol does not stimulate the circulation either by increasing the heart rate or by raising the blood-pressure. The advocates of the use of alcohol, while admitting the truth of the foregoing, may claim that whisky improves the circulation in some other fashion. Thus, this drug may increase the work done by the heart or it may increase the velocity of the blood flow or it may improve the efficiency of the heart as a pump. Lieb found that the changes induced by whisky in these three factors were comparatively insignificant.

**Acute Yellow Atrophy of the Liver in Syphilis.**—BENDIG (*München. med. Wchnschr.*, 1915, lxii, 1144) reports a case of primary syphilis who was being treated with both mercury and salvarsan. The first two injections of salvarsan were followed by no untoward symptoms, but the third injection produced marked vomiting, and two days later symptoms of acute yellow atrophy developed with a fatal termination within two days. Bendig calls attention to the fact that he reported in 1908 an almost identical fatal case. Since this was before the discovery of salvarsan he believes that salvarsan need not necessarily be the cause of death in the present case.

## PEDIATRICS

UNDER THE CHARGE OF

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OF PHILADELPHIA.

**Tuberculous Skin Lesions.**—NORTHRUP (*Arch. Pediat.*, 1915, xxxii, 887) reports a tuberculous skin eruption in a child of fifteen months. Three similar cases were reported previously. This condition is rather rare in the very young and Tileston concludes it occurs only in fatal cases as a terminal event. The case in point had tuberculous meningitis and pulmonary tuberculosis besides the skin lesions. There was a history of tuberculosis in the mother and a brother. The history shows progressive wasting for six months. The lymphatic glands of the neck, axilla and inguinal region were moderately enlarged. The skin eruption was mostly on the trunk, especially on the back, some on the face and forearm. The character of the lesions was papulopustular and umbilicated, and while showing no tubercle bacilli on microscopic examination, was diagnosed as a tuberculide of the skin with some secondary infection. There were tubercles in the lymph nodes and subcutaneous tissue, the lungs, meninges, and intestines. While no bacilli were found in the sputum, glands or skin lesions, the Roentgen-ray showed miliary tuberculosis of the lungs. The physical signs in the chest had been inconclusive. This exemplifies the important bearing the Roentgen-ray has on diseased conditions, especially in children. While localized tuberculosis is common, disseminated tuberculous eruption of the skin, necrotic tuberculid, is rare in infancy.

**Macewen's Sign in Intracranial Pressure.**—WILCOX (*Arch. Pediat.*, 1915, xxxii, 909) offers an interesting elucidation of Macewen's sign in changes and intracranial pressure and illustrates the practical application of this change of note. Different normal percussion notes belong to varying ages, with their corresponding states of skull development. Disease influences the character of skull percussion, rickets being the best example of this. A rachitic skull at six years

will give a percussion note similar to that found normally in an infant of six months. If this case develops increased spinal fluid a sharp, high-pitched, clear note is at once found to have replaced the former full, low-pitched, non-resonant percussion. If the cranial walls are too thin no note will be produced even though intracranial pressure be high. Macewen's sign is best determined by the stethoscope placed on the forehead just above the base of the nose. The skull is tapped directly with the percussing finger or hammer over the parietal region, beginning just over the parietal boss, from which the finger approaches the stethoscope. This should be carried out on both sides of the head. The typical sign observed in this way consists of a high-pitched, sharp, short, cracked-pot note. It is most distinct over and around the parietal boss and diminishes toward the stethoscope, while the reverse obtains in a normal skull where the note is heard more loudly as one approaches the stethoscope. The cracked-pot note of Macewen should be considered as a relative variation from the normal and not as a definite entity. When this sign is positive and cerebral fluid under pressure is withdrawn in the usual amount the note goes back to more nearly the normal almost at once. The sign was present in 50 of 53 cases of tuberculous meningitis and 17 of 18 cases of meningitis of other types. It was present in all of 5 cases of poliomyelitis. It was found to vary directly with the development and recession of cerebral symptoms as complications of disease not directly affecting the central nervous system. The sign is uniformly lacking in children normal as to the brain and its coverings.

**Infantile Paralysis in North Austria.**—STIEFLER (*Wien. klin. Wchenschr.*, 1915, xxviii, 1079) states that aside from very occasional sporadic cases, anterior poliomyelitis did not appear in epidemic form in Austria, especially the northern part, until 1907. Stiefler analyzed 187 cases occurring from 1909 to 1913. These cases are practically equally distributed among males and females. The highest number of cases occurred in children from three to six years of age (45 and 46 cases), the next highest being between four and six years (32 cases). The incidence decreases with increasing age periods, but between forty-one and fifty years 9 cases are reported. Most of the cases occurred among the farming and laboring classes. Almost all cases showed a prodromal stage of several days with fever, rarely chill, as the leading symptom followed by severe sweats, vomiting, and constipation, and later inflammation of the throat. Otherwise the respiratory system was rarely affected. Extreme tenderness of muscles and nerve trunks and paresthesias with pain in the legs and back are constant symptoms in these cases. Severe delirium occurred in only 11 cases. There was generally a leukopenia. Motor disturbances such as clonic spasm, tremors, and choreiform movements were frequently observed in paralyzed limbs. Under Zappert's classification these cases would be divided as follows: Spinal form, 148 cases; cerebral form, 12 cases; and abortive form, 27 cases. In the acute stage the paralysis affected mostly the lower extremities and in one-third of the cases the gluteal and back muscles were involved. Of 180 cases including the paralyzed and abortive cases 61 recovered completely, 93 recovered partly, and 23 died. Only 37 of the paralyzed cases recovered com-



pletely. The highest mortality occurred between the ages of seven and fourteen years. From the epidemiological standpoint the history of these cases offers no new features. The incubation period was estimated to be from six to ten days.

## OBSTETRICS

UNDER THE CHARGE OF

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**Pregnancy in a Rudimentary Uterine Cornu and in Bicornate Uterus.**—MICCABRUM (*Ann. di Osteter.*, 1915, No. 8) reports a case from Mangiagalli's Clinic in Milan and illustrates his paper with some excellent colored reproductions of microscopic sections. He finds a special and unusual arrangement of the muscle fiber in the rudimentary cornu in this case and that there is not present the usual arrangements of Langhans's layer. He found a direct connection between the rudimentary cornu and the maternal vessels through the intervillous spaces, nor did the vessels of the rudimentary uterus suddenly terminate in those of the decidua. There is a distinct decidua which forms in these cases and which seems to be developed largely from the muscular tissue. He does not consider that the conditions found are the result of mechanical factors nor that they are secondary to the anatomical peculiarities of the case. His study of the subject convinced him that the data ordinarily given as significant in the diagnosis of these cases are frequently of very little value.

**The Origin of Icterus in the Newborn.**—BANG (*Arch. mens. d'obstet.*, August, 1915) has studied this subject in the clinic at Copenhagen. He finds that the examination of the blood taken from the skin of the newborn soon after birth shows a great increase in the number of red cells. This must be considered a condition of stasis in the capillaries. During the first few days following birth the percentage of hemoglobin gradually, under normal conditions, returns to the average. Where, however, pathological conditions are present, the excess continues. The conditions are favorable for the retention of the excess in the liver, biliary pigments are formed in excess and absorbed throughout the entire organism.

**The Abderhalden Method of Diagnosis in Pregnancy in the Clinic at Basel.**—BAUMANN (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, xlii, 3) gives his experience in the obstetrical wards in the clinic at Basel. He obtained good results with the use of ninhydrin with placental tissue prepared by his own methods and by dialysis. He also had good results with what is known as dried placental albumin manu-

factured by the Hoechst method. Of this he employed 0.5 and 0.25 gm. in his experiment. When he used the moist placental substance, also devised by Hoechst he had 40 per cent. of failures. The substance known as color placental extract failed to give good results. He had especial success by the Abderhalden method in diagnosticating difficult cases where there was much uncertainty in differential diagnosis. Including cases of abortion and tubal molar pregnancy, the percentage of failures in diagnosis was from 3 to 4. If these were excluded, the percentage of failures diminished to 1.5 to 2 per cent. In one instance of tubal gestation, he took the blood direct from the open abdomen and believes that the negative reaction arose from a failure in the technic. In a second case of pregnancy and myoma which gave late negative reaction, it was impossible to tell the reason for the failure of the test.

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**The Abderhalden Reaction in Patients Who are not Pregnant.**—VAN WAASBERGEN (*Monatsschr. f. Geburtsh. u. Gynäk.*, 1915, xlii, 3) has made experiments with the Abderhalden test in patients not pregnant. In van der Hoven's Clinic in Leyden the writer examined the sera of 69 women not in the pregnant condition and who had some abnormality or some condition of ill-health. The sera were treated after the Abderhalden method, using the dialyzing apparatus; in order to make a test of the accuracy of the method he employed a 1 per cent. peptone to obtain the characteristic violet color with ninhydrin, before applying the method to the sera in question. The first test made showed that of the 69 sera but 7 gave a negative reaction, but the intensity of the positive reaction differed very greatly. It was interesting to observe that, in cases where there was a weak positive reaction, if the temperature arose, the reaction was very much stronger and that in the 7 cases giving a negative reaction, 3 changed to a positive reaction when fever developed. The 4 sera which remained negative were from patients who had passed the menopause and were suffering from prolapse, while the other 3 sera were from women aged respectively, fifteen, sixteen, and forty-one years. He divided the 68 patients into two groups, one aged from fifteen to twenty-five years; the other twenty-six years and more. In the first group there were twenty and of these 55 per cent. gave a positive reaction; 35 per cent. a weak positive reaction; 10 per cent. a negative reaction. In the second group there were 43 of whom 37.5 per cent. gave a positive reaction; 52 per cent. a weak positive reaction; 10 per cent. a negative reaction. These cases were again studied when some fever had developed and in the first group 90 per cent. gave positive reaction; 10 per cent. a weak positive reaction and none of them a negative. In the older group 50 per cent. gave a positive reaction; 41.5 per cent. a weak positive reaction; 8.5 per cent. a negative reaction. Evidently age had a considerable bearing upon the working of the test. The writer draws attention to LANGE's (*Berl. klin. Wchnschr.*, 1914, No. 17) experience, who obtained a positive reaction in patients suffering from tuberculosis and in surgical cases where pus had formed. As fever is accompanied by increased metabolism it is natural to expect a positive Abderhalden test when fever is present. The writer in 41 cases obtained the date at which the menstrual period was expected and these patients were

divided into three groups, in accordance with the time elapsing before the actual development of the period. As the time for menstruation approached it was found that the reaction grew more intense, while at the moment of menstruation or immediately after it again became much weaker. Hence the test is a positive indication that pregnancy is not present, but menstruation is approaching.

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**Disturbance in the Function of the Liver during Pregnancy.—**

BAUCH (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, xlii) has examined 22 pregnant patients by the administration of 40 gm. of galactose to determine the presence of this substance in the urine. In 8 (or 37 per cent.) there was the elimination of from 0.4 to 1.8 gm. which did not, however, exceed the amount which is found in healthy non-pregnant cases and should therefore not be taken as indicating a pathological condition. Unquestionably the amount of sugar in the blood increases during pregnancy, but hyperglycemia was not observed. In one case showing some symptoms of a mild pregnancy toxemia there was an increase in the sugar content of the blood and when galactose was administered this became noticeably greater.

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**Bed-sores Complicating Parturition and the Puerperal State.—**

KOTTMAYER (*Zentralbl. f. Gynäk.*, 1915, No. 39) reports the case of a primipara, aged twenty-six years, delivered spontaneously who, on the second day after labor, showed in the region of the posterior superior spine of the ileum two bluish-red surfaces which developed into bed sores. The patient had also sustained a laceration of the perineum and stitches had been taken, but this lesion healed slowly and poorly and it was necessary to keep the patient quiet in bed for twelve days. During this time, the bed sore healed under aseptic precautions and the use of ointments. His second case was that of a small, pale, primipara with contracted pelvis, who gave birth to a child in spontaneous labor and in the latter portion of the labor became very excited with greatly increased patellar reflexes and great irritation of the skin. On the second day after the birth of the child in the same region similar lesions developed to those described in the first case. This patient had a gonorrheal endometritis and was three weeks in bed and all of the lesions during that time disappeared. His third case was also a primipara and in vigorous health, delivered spontaneously with considerable laceration of the pelvic floor and perineum. The child and the pelvis were disproportionate and the mother's pains became excessively strong during the latter part of labor. A vesicovaginal fistula developed on the second day which closed on the fifth day with the use of a permanent catheter. After the second day following the birth of the child a reddened area developed over the sacrum which became a bed sore in three days. Its border became well marked and on the sixth day a superficial slough was discharged after which the lesion gradually healed. On the same day when this appeared the patient had left-sided herpes labialis. There was no sudden rise in temperature and the general condition remained good. The reflexes were much increased and there was considerable irritation in the skin. The fourth case was a vigorous primipara with a rachitic and contracted pelvis, not sufficiently small to prevent spontaneous labor. On the day following the birth of the child, there was the development

of a well-defined reddened area over the sacrum and in the two following days, a slough formed and the surface ulcerated which required three weeks' treatment to heal. In these cases, the question naturally arises whether the constant pressure of the abdominal binder can have anything to do with the lesions described. This connection cannot be considered as proven. Those who have reported similar cases have considered them as toxic and that the patient had some predisposition to irritation of the skin which made this occurrence possible. The increased reflexes and irritation in the cutaneous nerves point also to some abnormal state of the nervous system and this is borne out by the fact that these lesions developed in patients who had strong uterine contractions and considerable suffering during labor.

**The Indications for Abdominal Cesarean Section.**—In a recent book KÜSTNER (*Deutscher Frauenheilkunde*, 1915, ii), in treating of abdominal Cesarean section, naturally considers the indications. First he puts considerable pelvic contraction. This brings the operation into comparison with hebosteotomy, the induction of labor, prophylactic version and the high application of the forceps. As regards repeated section, Küstner does not believe that because a Cesarean section is performed, that sterilization should be done at that time. If a second section becomes necessary, sterilization should also be considered when the uterine scar is found very thin and weak. In his experience, he would often perform the extraperitoneal section for the first and second operations and if the operation was repeated for a third time, he would accompany it with sterilization. He is not in favor, because a pregnant woman has a myoma, of removing the uterus and thus destroying the pregnancy with the removal of the tumor. He believes that Cesarean section is rarely indicated in myoma complicating pregnancy. Rupture of the uterus he believes to be a valid indication for the operation. Should such a patient recover by the suture of the lacerated surface in the uterus, the danger of repeated rupture in a following pregnancy is very great. In cases where a vesicovaginal fistula has required a difficult operation for closure and the patient subsequently becomes pregnant, he would deliver by section when the pelvis is contracted and the fistula was so situated that delivery through the cervix would probably cause the formation of a second fistula. He does not believe that illy developed soft parts or a resisting pelvic floor indicate abdominal Cesarean section. In these cases, as in eclampsia, he would use deep incisions as necessary. In placenta previa complicated by contracted pelvis, profuse hemorrhage and where there is reason to believe that the patient is not infected, Cesarean section would give good results. Many cases of placenta previa are successfully treated by the use of the dilating bag. Abnormalities in the mechanism of labor when they occur in patients having moderately contracted pelvis rarely indicate Cesarean section. So, especially if the child is dead, craniotomy should be performed. Where the normally situated placenta becomes misplaced, vaginal section is the operation of choice. As a general rule, abdominal Cesarean section is indicated where it is evidently dangerous and difficult to empty the uterus through the vagina. When the circumstances are thoroughly known and the diagnosis of rapidly impending death is sure, abdominal Cesarean section of the dying may be permitted.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Vaginal Supravaginal Hysterectomy for Procidentia.**—This operation is advocated by VINEBERG (*Surg., Gynec. and Obst.*, 1915, xxi, 741) for use in those cases where the interposition type of operation would be used were it not for the presence of some contra-indication, such as the presence of fibroids or of uncontrollable uterine hemorrhage, thus necessitating the removal of the uterine body. Instead of doing a vaginal panhysterectomy in these cases, Vineberg does a supravaginal amputation through an anterior vaginal incision, then utilizing the cervical stump as a *pelote* to hold up the bladder. The amputation may be done high enough, if desired, to leave sufficient endometrium for maintenance of subsequent menstruation, the adnexa of course being not removed. If the cervix is greatly elongated, as is frequently the case, Vineberg amputates the lower portion of this as well, leaving only a comparatively short cervical stump, extending from the vaginal vault to the lower uterine segment, to be utilized for the bladder support. After the redundant vaginal flaps are resected, the cervical stump is sutured to the subpubic fascia and the anterior vaginal wall, thus forcing the bladder to take a position within the abdomen, and prevent its prolapse. The operation is completed by repair of the perineum. The author reports having performed this operation ten times, the first over three years ago. Excluding 2 very recent cases, and 1 that was lost sight of, the remainder have been under observation for periods varying from eight months to three years and three months, with excellent anatomic results in all, and equally good clinical results in all but 1. This patient continued to complain of an uncomfortable bearing-down feeling and frequent micturition, although there was no recurrence of the rectocele.

**Acute Torsion of the Normal Tube and Ovary.**—A case of this extremely rare condition has been recently reported by BARRINGTON (*Jour. Obst. and Gynec. Brit. Emp.*, 1915, xxvii, 141). The patient was a married woman, aged thirty-eight years, who had had twelve children, attended by various complications, the last having been delivered by Cesarean section seven weeks previous to the onset of the ovarian condition. The latter manifested itself by a sudden attack of severe pain in the abdomen while the patient was walking upstairs, gradually getting worse, and localizing to the right iliac region. Almost immediately diarrhea set in, soon followed by vomiting. There was no vaginal bleeding. The pain persisted throughout the night, but was much less severe the following day. On admission to the hospital the patient's abdomen showed no tenderness or rigidity, except on deep pressure in the right iliac region, which did elicit considerable

tenderness. On rectal examination, a lump could be felt above the cervix, independent of the uterus. About twenty hours after the onset of symptoms the abdomen was opened, revealing some excess of clear, not blood-stained fluid in the peritoneal cavity. The appendix was normal, but a tense, elongated lump was left lying behind the uterus to the right of the midline, with its lower extremity at the bottom of Douglas's pouch. On further investigation, this lump was seen to consist of the right ovary, which with the distal part of the tube was twisted on its pedicle at least one complete turn; there were no adhesions to the ovary or uterus. The right adnexa were removed, the left, which appeared entirely normal, being allowed to remain undisturbed. On examination after removal the ovary was found to be about twice the normal size, its surface uniformly blackish-purple in color; the part of the tube distal to the twist was dark red. A vertical section through the ovary showed the parenchyma to be stained throughout dark red from hemorrhage, but the Graafian follicles and a corpus luteum were preserved and were not invaded by the hemorrhagic infiltration. The question as to any possible etiological relation between the antecedent Caesarian section and the subsequent development of this extremely unusual ovarian lesion is unfortunately not mentioned.

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**End-results of Nephrectomy for Renal Tuberculosis.**—An interesting study of the ultimate fate of patients subjected to nephrectomy for renal tuberculosis has been made by CRABTREE (*Surg., Gynec. and Obst.*, 1915, xxi, 669) from the records of the Massachusetts General Hospital. In a series of slightly over 100 cases there was a primary operative mortality of 4 per cent., with a late mortality of 20 per cent., (about half the deaths furnishing this "late mortality" occurred within two years, and the remainder within five years after operation). The author considers that only about 60 per cent. of the cases can be considered cured of active tuberculous lesions at the end of five years, the remaining showing residual symptoms, such as nephritis, possibly of toxic origin, irritable bladders, pyuria, etc. In about 10 per cent. the course of the disease was apparently in nowise checked by the removal of the kidney. An extremely interesting, and rather surprising point, brought out by Crabtree's statistics, is that apparently in many instances very early cases, with comparatively slight destruction of kidney tissue, do worse than more advanced cases, with more extensive disease. A possible explanation for this apparently anomalous condition is offered in an introduction by Cabot, on the ground that it may "depend on at least two conditions: (1) that the renal tuberculosis is only an evidence of a generally low resistance to the tubercle bacillus, and that the failure of nephrectomy to control the process proved nothing except that it could not have been controlled by any method; (2) that the process in the kidney is so early that there has developed no immunity, and that if left to itself for a short time, such heightened resistance might come. . . . While it would seem a pity to do anything which remotely tended to discourage the only just developing enthusiasm for removing the tuberculous kidney at the earliest possible moment, it is clearly necessary to call attention at the present time to what our experience has led us to believe to be a not inconsiderable danger, viz., the lack of resistance in patients with early tuberculous

lesions of the kidney." Another interesting point brought out, is that in about 75 per cent. of cases sinuses develop, irrespective of whether the wound is drained or closed tight, the sinus development in the latter class occurring rather late, however, after apparent healing, so that had not a follow-up system been employed, the apparent results of this technic would have been much better than was actually the case. Secondary complications, especially involvement of the genital tract, were much less frequent in women than in men, and the prognosis in the former therefore considerably better.

**Fatal Mercury Poisoning from Vaginal Douche.**—A rather remarkable case, in which death resulted apparently from the systemic effects of mercury absorbed through the vaginal mucosa following the employment of a strong solution as a douche, is reported by FOSKETT (*Am. Jour. Obst.*, 1915, lxii, 639). The patient was an unmarried girl of twenty-two years, who took a douche consisting of three of the ordinary 7.3 grains bichloride tablets dissolved in a cup of water, and administered by means of a whirling spray. She felt a burning sensation in the vagina at once, accompanied by general distress. By the third day her condition was so serious that she was removed to a hospital. At this time the vagina and vulva were covered by a white sloughing surface; salivation was present, and the mucous membranes of the mouth and pharynx were also white and sloughy. Urinary output was as low as from 1 to 2 ounces per twenty-four hours for three days, after which it gradually came up. The urine contained albumin, granular and hyaline casts, but no mercury. On the seventh day the vaginal slough separated, followed by some bleeding. Soon after this hiccoughs and vomiting appeared, followed by bleeding from the nose and mouth, with sore throat, restlessness, and mental disturbances. The general condition grew steadily worse, incontinence developed, with blood in vomitus and stools. Death occurred on the twelfth day.

## HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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**Some Results of the First Year's Work of the New York State Commission of Ventilation.**—A preliminary report of the Commission has been published by C. E. A. Winslow (chairman), D. D. Kimball, Frederic S. Lee, J. A. Miller, Earle B. Phelps, E. L. Thorndike, members

of the Commission, and G. T. Palmer, chief of the investigating staff (*Amer. Jour. Public Health*, February, 1915). Two problems studied by the Commission are reported on: (1) results obtained in regard to the effect of temperature and humidity upon physical and mental condition and efficiency, and (2) results in regard to the effect of carbon dioxide and organic matter in stagnant air on both physical and mental condition and efficiency. The experimental work was carried out in specially equipped ventilation laboratories at the College of the City of New York. Ninety-three paid college students acted as experimental subjects. These were observed in the room over four- to eight-hour periods during the day in seven different series of experiments each of which lasted from one to eight weeks. The effects of temperature conditions of  $86^{\circ}$  with 80 per cent. relative humidity, and of  $75^{\circ}$ , 50 per cent., and  $68^{\circ}$ , with 50 per cent. relative humidity were compared. The effects of carbon dioxide and stagnant air as compared with fresh air were studied by keeping the temperature and humidity constant and supplying no air at all or 45 cubic feet per minute per person.

*Effect of environmental temperature:* The bodily responses observed and the results obtained are here given: (1) *Body Temperature:* Room temperature of  $68^{\circ}$ ,  $75^{\circ}$  and  $86^{\circ}$ , have slight but definite effects on the rectal temperature. The average of 284 readings, taken at the end of a four- to eight-hour stay in the observation room at  $68^{\circ}$  was  $36.73^{\circ}$  (range,  $36.50^{\circ}$  to  $39.96^{\circ}$ ), the drop from initial temperature being  $0.19^{\circ}$  to  $0.80^{\circ}$ . (Room temperature, T; body temperature, C). Similarly, 119 final readings at  $75^{\circ}$  gave an average of  $36.99^{\circ}$ . (range  $36.58^{\circ}$  to  $37.10^{\circ}$ ), a fall in body temperature in four series of  $0.08^{\circ}$  to  $0.44^{\circ}$ , or a rise, obtained in one series, of  $0.19^{\circ}$ . One hundred and ninety-nine final observations at  $86^{\circ}$  averaged  $37.41$  (range  $37.08^{\circ}$  to  $37.56^{\circ}$ ). In two series there was a rise of  $0.15^{\circ}$  to  $0.43^{\circ}$  from the initial temperature and in three a fall of  $0.01$  to  $0.05^{\circ}$ .

*Pulse:* Exposure to a  $68^{\circ}$  temperature for four to eight hours caused an average fall in pulse rate of 11 to 13 beats. A  $75^{\circ}$  or  $86^{\circ}$  temperature gave a drop in three series of 2 to 5 beats, and in 3 cases an increase of 1 to 4 beats. The average for all observations shows that the pulse under the  $86^{\circ}$  condition was 8 beats per minute higher than under  $68^{\circ}$ , which was 66.

*Increase in heart rate on standing:* The average increase in heart rate on going from the reclining to the standing position was 10 beats per minute at  $68^{\circ}$ , 21 beats at  $75^{\circ}$ , and 25 beats at  $86^{\circ}$ .

*Pulse recovery after physical work:* A slower pulse recovery after physical exertion was found to exist under a  $75^{\circ}$  condition as compared with a  $68^{\circ}$  condition.

*Systolic blood-pressure:* The average of all blood-pressure readings taken by the auscultatory method at the end of the period in the chamber was 116 mm. for the  $68^{\circ}$  and  $75^{\circ}$  and 112 mm. for  $86^{\circ}$ .

*Crampton value:* The Crampton index of vasomotor efficiency is based on the relation between rise in pulse and change in blood-pressure on going from a reclining to a standing position. Using an arbitrary scale in which a high value is given to an increase in blood-pressure accompanied by only a slight increase in heart rate the Crampton values were 60, 45, 40, 35 as a result of staying in the room under a  $68^{\circ}$ ,  $75^{\circ}$ ,  $86^{\circ}$  (with fans), and  $86^{\circ}$  condition respectively. The highest vasomotor efficiency existed at a low temperature.

*Respiration:* One minute respiration counts which were made under the different temperature



conditions gave no positive results. *Special physiological studies:* The different room temperatures were found to have no effect on the size of the dead space in the lungs, or on the acidosis of the blood, respiratory quotient, rate of digestion, heat production, creatinin in the urine, freezing-point, or specific gravity of the urine, showing that profound metabolic changes did not take place. *The quantity and quality of intellectual products and the inclination to do mental work* were studied by standardized psychological tests and by mental tests in which the subjects could either work or idle. Neither the amount or quality of the work accomplished or the desire to do the mental work were markedly affected by the different temperatures. *Inclination to do physical work:* When the subjects were required to ride a bicycle ergometer or when they had the option of working with dumb-bells for pay or idling they accomplished 15 per cent. more work in the fall at 68° as compared with 75° and in the summer 37 per cent. more work at 68° than at 86°; although the ability to work under pressure was not affected. *Appetite:* The appetite was slightly affected by temperature. In two separate series 1.5 per cent. more food was consumed at 68° than at 75° and 5 per cent. more at 68° than at 86°. *Comfort:* The votes as to comfort, which were based on a scale of five conditions, showed that in general the subjects were more comfortable at 68° and 75° than at 86°. *Effect of carbon dioxide and stagnant air:* In five series of experiments using a total of thirty-six subjects over eighty-five days, a comparison of the effect of breathing fresh air and stagnant air gave practically negative results. At the end of the stagnant days the average CO<sub>2</sub> proportion in the air was 37.9 parts per 10,000; on fresh air days seven parts per 10,000. All of the physiological and psychological responses mentioned above were found to be uninfluenced by the chemical purity of the air except the appetite. In one test 13 per cent. more food was consumed at 68° than at 86°, and in another 8.6 per cent. more at 68° than at 75°. This indication of a positive result is not entirely borne out in additional experiments now under way. The broad, tentative conclusions of the Commission based on this first year's work are: high temperatures, such as 86° and 75°, cause an increase in body temperature, in the reclining heart rate, in the excess of standing over reclining heart rate, and a slight diminution in systolic blood-pressure, and a fall in vasomotor tone but no fundamental metabolic changes. Desire for physical work is decreased at high temperatures, but mental ability is unaffected. Stagnant air at the same temperature as fresh air and without a disagreeable odor has no effect on the mental or physiological functions of the body except perhaps on the appetite for food.

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**State Control of Sewerage Systems.**—According to the U. S. Public Health Report for October 29, 1915, the Supreme Court of Maryland has held that the section of the act of the Maryland Legislature, passed in 1914, giving the State Board of Health authority over the installation of water and sewerage systems, was not unconstitutional. The act empowered the State Board of Health to order the local authorities to install public systems of water supply, sewerage, or refuse disposal, in any county, municipality, district, subdivision, or locality where the absence or incompleteness of such systems were, in the opinion of

the State Board of Health, sufficiently prejudicial to the health and comfort of the community. The act further provided that local authorities, if they deemed any such order unlawful, unreasonable or unnecessary, might bring action in court to set aside the order. It seems that the State Board of Health in 1914 ordered the county commissioners of Baltimore County to install a sewerage system in a certain section of that county, stating that the absence of such a system was a menace to the health of the people. The commission brought suit to have the order set aside, and attacked the constitutionality of part of the law, but did not claim that the order was unreasonable.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Experimental Studies on Adrenal.**—A series of studies was undertaken by CROWE and WISLOCKI (*Brun's Beitrage*, 1914, xcv, 8) on dogs. The adrenal is a vital organ for these animals and it would appear that the cortex is more important than the medulla. After partial extirpation the remaining portion undergoes hypertrophy, which is mainly confined to the zona fasciculata. The medulla shows no hypertrophy. After an almost complete bilateral extirpation the animals frequently have convulsions and subnormal temperature. In a few instances the animals recover without evidence of ill effect and absence of disturbances of growth or sexual function. A transient glycosuria is commonly observed in the experiment. There appears to be some relation between the adrenals and the lymphatic system. Occasionally there is a hyperplasia of the thymus. Acute general infection may cause focal necrosis in the cortex.

**Studies of the Pathology of Osteogenesis Imperfecta.**—The bone affections in rickets, osteomalacia, osteoporosis, scurvy and osteogenesis imperfecta are more or less related inasfar as each is dependent upon metabolic disturbances. The development of characteristics of one or other type is in part dependent upon a predisposition as well as the peculiar metabolic derangement presenting. HART (*Ziegler's Beitrage*, 1915, lix, 207) reported a case which he found considerable difficulty in classifying. A boy, aged twelve years, had, during five previous

years, taken quantities of alcohol and developed glycosuria and obesity with furunculosis. At the age of nine years atrophy and fragility of the bones developed to the degree that great deformity of the vertebrae and ribs appeared. Numerous fractures of the long bones occurred with favorable callous formation. Microscopically there was an absence in the callous of proper bone formation and osteoblasts did not appear to actively participate in the reaction. An irregular calcareous deposition took place in the injured areas. The author looks upon this case as one of osteogenesis imperfecta in which osteomalacia could not be entirely ruled out. The author suggests that in part the disturbance of the bone tissue was brought about through the unusual development of fatty tissues in the bones. There was no evidence that the endocrin glands were at fault. The author believed that this individual was possessed of an abnormal constitution whose peculiarities were only demonstrated through the influence of alcohol. Thus osteogenesis imperfecta need not always appear as a congenital disease, but its predisposition may only manifest itself in the presence of particular constitutional derangements in postnatal life.

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**Histological and Experimental Observations on the Destruction of Tumor Cells in the Bloodvessels.**—Various authors have studied the fate of tumor cells in different tissues. At times, individual tumor cells are destroyed by the phagocytosis of giant cells, at other times a lytic destruction leads to a spontaneous disappearance of small tumor masses. Such methods of tumor cell destruction are now well recognized so that it is fully appreciated that each tumor cell liberated from the main mass does not necessarily survive. IWASAKI (*Jour. Path. and Bacteriol.*, 1915, xx, 85) studied a number of human malignant tumors including cancer, sarcoma, and hypernephroma, observing particularly the character of tumor emboli. These emboli are either naked, covered with recent clot or show an advancing organization of the blood clot around them. Within each type various grades of necrosis beginning in the centres were found. The destruction of the tumor cells occurs either through want of nutrition or by the unfavorable character of the granulation tissue. Nevertheless, tumor masses may remain latent for long periods of time. The author also carried out a series of experiments in which the Jensen tumor was inoculated intravenously with mice. The vascular emboli were subsequently studied and in general their fate was similar to that of the human. The author believes that there is a special affinity between tumor cells and the cells of certain organs.

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**Contributions to the Pathology of Lipomatosis.**—One of the most common disturbances of tissue metabolism is found in the varying accumulation of fat in the interstitium. MATSUOKA (*Jour. Path. and Bacteriol.*, 1915, xx, 106) studied the development of fat tissue under a variety of conditions from infancy to old age. It is readily appreciated that no definite division between the physiological and pathological deposits of fat tissue can be determined. The lipomatosis may be general or localized. Under some conditions lipomatosis appears to be a progressive process whereby the fatty tissue is superimposed upon the tissues of an organ. On the other hand, lipomatosis also develops

in consequence to an atrophic process. In the latter, the primary atrophy is usually associated with fibrosis in which the fatty tissue appears to take its origin. The author believes that the fat cells are nothing more than modified connective-tissue cells. He, however, offers no evidence for these conclusions. During the development of local or general lipomatoses the involved area shows an unusual hyperemia

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**Atrophy in Adipose Tissue and the Histogenesis of Fat Cells.**—MATSUOKA (*Jour. Path. and Bacteriol.*, 1915, xx, 118) claims that atrophy of adipose tissue is common, and that one may quite readily distinguish the degree of atrophy by the contour of the shrinking cells. Fat atrophy is commonly accompanied by an increase in the connective tissues. The early stages, however, show a serous infiltration. This infiltration is made possible through the great vascularity of adipose tissue. In the proliferation of fat cells "the old fat drop becomes absorbed and deposited in the young cell." The nucleus shows a definite activity in the metabolism of fat and in true fat cells globules of sudan-staining material are present in the nucleus. The lobulated adipose tissues can be converted into bundles of spindle-shaped connective-tissue cells, and for example, the whole epicardial fat which is derived from fibrous tissue, can be reconverted into such connective tissue. Thus fat cells of every kind result from a metaplasia of connective-tissue cells.

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**Chronic Interstitial Nephritis and Tuberculosis.**—The influence of tuberculosis in leading to a chronic interstitial nephritis has been suggested by a number of observers. SCHOENBURG (*Virchows Archiv*, 1916, cxxx, 285) reports a second series of cases supporting his previous view on the importance of tuberculosis in bringing about chronic fibrotic processes in the kidney. These lesions are seen at all periods of life, but the more interesting ones occur in the second and third decade where a histological analysis more clearly demonstrates the origin of the process. The kidney lesion may appear in the form of isolated scars or diffuse fibrosis. The former are the result of tuberculous processes about the arteries whereby circulatory disturbances lead to hyaline degeneration of the glomeruli and atrophy of tubules of cortex. This type of lesion simulates the arteriosclerotic kidney. In the second type the process is more diffuse and the fibrous tissue is more evenly distributed. Here the glomeruli are less involved while a general atrophy of the cortical tubules is found. Commonly the two conditions are seen in the same kidney.

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ORIGINAL ARTICLES

CONGENITAL AND ACQUIRED ENURESIS FROM  
SPINAL LESION.

(a) MYELODYSPLASIA. (b) STRETCHING OF THE  
CAUDA EQUINA.

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**MYELODYSPLASIA.** Under the name of myelodysplasia, Alfred Fuchs,<sup>1</sup> in 1909, described anomalies of development, and enuresis nocturna, associated often with spina bifida occulta, and depending on imperfect development of the lower part of the cord. The important features of this condition are:

1. Weakness of the sphincters and especially enuresis nocturna persisting after puberty.
2. Syndactylism between the second and third toes, more rarely between the second, third, and fourth toes, still more rarely between the other toes; usually bilateral.
3. Disturbances of sensation, chiefly of temperature sensation, not strictly radicular in type, especially in the feet and more frequently only in the toes.
4. Defect of the sacral canal recognized by the Roentgen-rays.
5. Anomalies of cutaneous and tendon reflexes in the abdomen and lower limbs.
6. Defects in the feet in many cases (pes planus, varus, valgus), sometimes with peroneus weakness, also trophic and vasomotor disturbances in the toes.

<sup>1</sup> Wien. med. Wchnschr., 1909, p. 2111.

Other anomalies that should be sought for are hypertrichosis of the sacral region, lipoma in the coccygeal region, asymmetry of the rima ani, fovea coccygea, or fistula-like depression of the sacrococcygeal region.

Mattauschek studied with Fuchs 24 adults with enuresis (20 soldiers and 4 civilians) and found anomalies in 21, which seemed to indicate hypoplasia of the conus.

Peritz and Saar observed by means of the Roentgen rays in 20 adults with enuresis and 20 children afflicted with the same disorder that 68 per cent. of the adults and 35 per cent. of the children had spina bifida occulta.

Lewandowsky has objected that spina bifida and enuresis are merely associated conditions (cited by Vorkastner.)<sup>2</sup>

Peritz<sup>3</sup> believes that these conditions occurring in the same person have a relation to one another, because anomalies of the sacrum are found in 68.2 per cent. of cases of enuresis in adults; because of thermo-anesthesia on the plantar surface of the toes, and of anomalies in the reflexes with enuresis. He states that 50 to 55 per cent. of children who have enuresis nocturna have it because of myelodysplasia.

Alfred Saenger,<sup>4</sup> since the report made by Fuchs, has examined every case of enuresis nocturna with roentgenographs, but has found only one in which myelodysplasia existed. His patient was a girl, aged eighteen years, who had complained of nocturnal enuresis a long time. She had no difficulty in holding the urine during the day. The enuresis had increased in later years. The right Achilles reflex was absent, a zone of diminished sensation in all forms was about the anus, and the Roentgen-ray picture revealed a defect of the sacrum.

Most cases of enuresis nocturna, he thinks, can not be attributed to myelodysplasia.

An unsigned (except for the initials J. C.) review of the myelodysplasia of Fuchs has been published recently in the *Archiv. de méd. des enfants*, August, 1915. Reference is made to three observations recently reported by C. Bonorino-Udaondo and Mariano R. Castex.<sup>5</sup> As these cases were observed in Buenos Aires and are published in an inaccessible journal I have abstracted them from the review.

CASE I.—Boy, aged fourteen years, had nocturnal and diurnal incontinence of urine since early infancy. The diurnal incontinence disappeared about the age of six or seven years, but the nocturnal incontinence persisted, and occurred only in sleep. He had certain malformations, cephalic and facial hypertrichosis, ogival palate,

<sup>2</sup> Handbuch der Neurologie, Lewandowsky.

<sup>3</sup> Deutsch. med. Wehnschr., July 6, 1911, p. 1256.

<sup>4</sup> Deutsch. Ztschr. f. Nervenhe., xlvii and xlviii, 694.

<sup>5</sup> Review de la Soc. méd. Argentina, November and December, 1914.

skeletal malformations, syndactylism of the feet, sensory disturbances confined to the big toes, and congenital valvular disease of the mitral orifice with hypertrophy of the right ventricle.

Motility was well preserved in the four limbs and trunk. The tendon and cutaneous reflexes were normal. Sensation was normal, except that thermic sensation was considerably diminished in the dorsal and plantar surfaces of the big toes. An interdigital membrane between the second and third and the third and fourth toes of each foot was pronounced (syndactylism).

Palpation over the vertebral column in the lumbar region revealed at the lower part of this region a slight oval depression, measuring 3 cm. in vertical diameter and 2 cm. in transverse diameter. Pressure here caused severe pain, and gave the examiner the impression of fibrous and not bony tissue. The defect implicated the lower lumbar vertebræ and sacrum, and was well shown by the Roentgen-rays. The pelvis was also deformed. The Wassermann reaction of the blood was positive.

CASE II.—Youth, aged twenty years, had a condition similar to that in Case I. He had nocturnal enuresis, small forehead, ogival palate, general and sexual infantilism, syndactylism, disturbance of sensation in each big toe, and congenital mitral valve lesion.

CASE III.—Boy, aged eleven years. He had pain in the legs, nocturnal enuresis from time to time, infantilism, thermic anesthesia of the big toes, syndactylism in each foot, and defect of the lowest lumbar vertebra and sacrum.

In all three cases the findings were: nocturnal enuresis, skeletal malformations, infantilism, ogival palate, cephalofacial hypertrichosis, syndactylism, and sensory disturbances in the big toes.

Whether defective development of the lower parts of the cord without defect in the sacrum and lumbar vertebræ is a common cause of enuresis nocturna with or without the described anomalies of development can not be determined without necropsies, and as yet sufficient attention has not been directed to this subject to enable us to form positive conclusions.

It is important to remember that the enuresis of older children and adults, not necessarily merely nocturnal, may occasionally be a sign of spina bifida occulta, and may exist without other signs or with few signs of this defect. Examination of the sacrum and lower lumbar vertebræ by means of the Roentgen-rays will readily determine a defect in these parts if it exist, and such a defect should warrant the physician in assuming that much exercise of the lower limbs might be followed by muscular palsy in the peroneal nerve supply. This is true in cases where pronounced spina bifida occurs, as in a case referred to me by Dr. Edward Martin, March 27, 1909. Had the young man avoided training for severe rowing he might not have developed all the serious symptoms he presented. The evident spina bifida should in itself have been a warning.

Still more important is the second case, in which the statement made by the boy that for years he had had enuresis led me to request a Roentgen-ray photograph of the sacrum and lower lumbar vertebrae from Dr. Pancoast. This patient gave no appearance of spina bifida to the sight or touch of the examiner, except some tenderness on deep pressure over the sacrum, but the Roentgen-rays showed a serious defect of the sacrum and lower lumbar vertebrae. The paralysis that developed from the comparatively light exercise of a bicycle ride of an hour and a half might have been avoided had the spina bifida occulta been suspected from the persistent enuresis.

CASE I.—*Pronounced spina bifida with enuresis and other symptoms increased by violent exercise.*

A. B., aged eighteen years. About two years previously to 1909 he had been in training in rowing, and he thought he had overtrained. It had become necessary for him, probably because of the training, to urinate often, and he had difficulty in holding the urine. He was obliged to urinate once every hour or even oftener. About 1905 he noticed that the toes of the left foot were becoming flexed, and the tendons of the toes and the Achilles tendon were cut. The left lower limb became weaker than the right and the left leg below the knee smaller. The right lower limb had not been affected. The bowels were regular, the power of erection was not affected, and seminal emissions at night occurred about once every three weeks. He had never had sexual intercourse, and there was apparently no implication of the nerve supply for the sexual functions.

Dr. Martin had obtained the statement that the urine was discharged in gushes resembling the rhythmical contractions of the gluteal muscles. A short time before my examination the patient on one occasion had tonic spasm of the abdominal muscles, at which time he had difficulty in getting his breath.

I found the left lower limb below the knee, including the foot, much smaller than the right, and there were marked fibrillary tremors below the left knee on the inner side of the leg. These were not observed elsewhere. The left toes were partially flexed. The left calf measured 30.5 cm., the right calf 35.5 cm. in their greatest circumference. The left thigh was a little atrophied in its inner part. Slight diminution of touch, pain, and temperature sensations was observed over the right buttock near the anus, but the impairment of these sensations was greater over the left buttock and in a band down the back of the left thigh as far as the knee. The patellar reflex was a little diminished on each side, and the Achilles reflexes were lost. There was no Babinski reflex. The limbs showed no abnormal tonicities, and there had not been pain. A spina bifida was observed over the sacrum. When the young man consulted me he was having constant dribbling of urine.



CASE II.—*Spina bifida occulta with enuresis and other symptoms developing after moderate exercise.*

R. C., aged fourteen years, was referred to the University Hospital by Dr. F. Bloomhardt, of Altoona. He was at first in Dr. Stengel's service, but was kindly referred to my service.

About May 1, 1915, the boy noticed some weakness in both feet. He could not run well, the toes dragged a little on the ground, but no illness preceded the onset of these symptoms. His family, however, noticed no disturbance until Memorial Day, at which time, after a three-mile bicycle ride, the boy found that the weakness of the feet was becoming pronounced, but he had no weakness at the knees or hips. The condition gradually improved slightly, and he recovered some motion in the toes and ankles, especially in the right leg. He never had any pain or paresthesia. When he came to the hospital he stated that he had always had difficulty in retaining the urine, although he never had pronounced incontinence. He had incontinence of feces on one occasion.

The examination about four months after the bicycle ride showed that all the symptoms aside from the enuresis were confined to the lower limbs. The muscles of the thighs were in fair condition. The legs below the knees were somewhat wasted and there was bilateral foot-drop. The power of spreading the toes had been lost. Dorsal flexion was almost abolished in both feet, and plantar flexion was impaired in the left foot. The patellar tendon reflexes were diminished and the Achilles reflexes were lost. Tactile sensation was normal. Pain sensation was impaired along the outer edge of the sole of the left foot and on the plantar surface of the toes.

The back in the lumbar and sacral regions appeared to be entirely normal to sight and palpation, except that slight tenderness could be elicited by deep pressure over the sacrum. The Roentgen rays showed a grave defect of the sacrum and lower lumbar vertebrae.

In this connection reference may be made to an interesting case of spina bifida reported by Tutyschkin, *Neurologisches Centralblatt*, February 1 and 15, 1914.

ENURESIS FROM STRETCHING THE CAUDA EQUINA. Disturbance of micturition may be acquired by stretching of the lower sacral roots in bending the trunk far forward on the lower limbs. In such a position the lower roots are severely stretched, and although the bending of the spinal column may be chiefly in the midthoracic region, the lower roots of the spinal cord are likely to be more affected than any others. These roots are the longest and the stretching is more severe in them. An interesting example of this accident is shown by the following case:

CASE III.—J. C., aged forty-six years, was referred to the University Hospital October 12, 1915, by Dr. J. R. Thompson, of Pittston. About nine or ten years ago while working in the shaft of a mine and stooping over, an elevator descended upon him and

he was caught beneath it. He sustained very severe pressure in such a manner that his trunk was bent forward on the lower limbs and his sight was affected for a time, but he was not made unconscious. He was taken home and kept on a lounge for several days, but was not paralyzed in the lower limbs. He returned to the mine about a week after the accident, walking with the aid of a stick.

Difficulty in retaining the urine and feces began soon after the accident and persisted about a year. He had incontinence of urine at night at times, but now has no difficulty in retaining the urine unless he has taken cold. He gets up once or twice at night to urinate, and during the day he voids urine more frequently. He has no loss of sexual desire, but power of erection has been lost, and he has no seminal emissions. The Achilles reflexes are lost, the right patellar reflex also is impaired, and the left patellar reflex seems a little exaggerated. He has some indication of Romberg's sign. Pain and tactile sensations about the anus and in the perineum are normal, as in the lower limbs.

A case that I reported in 1907<sup>6</sup> before the Philadelphia Neurological Society is similar to the one just described. The view has been held by some that hemorrhage might be the cause of the symptoms in such a case, but it is difficult to understand why the hemorrhage should occur only in the conus of the cord when the arching of the body is above this region, and in a case where the symptoms are unilateral, as in the following, hemorrhage seems improbable. Of interest in this connection is the report by Bittorf<sup>7</sup> of a man who while striking a heavy blow on an object between his feet missed the object and the blow went farther than he intended and caused paralysis of the sciatic nerve, probably from stretching of the nerve in the bending of the body forward, although hemorrhage into the nerve may have occurred.

H. C., a male, aged thirty-one years, was injured eighteen months previous to my examination by a bale of cotton falling against the abdomen. He was unable to work for about three weeks, but then returned to heavy work, feeling not quite so well as formerly. About a month after returning to his occupation, while lifting a bale of cotton, he "felt something give way" in the right inguinal region, and at the same time he heard a tearing sound. It is uncertain what this was. He immediately felt weak and limped on the right lower limb, but walked home, a distance of about two blocks, and went to bed. After one day he got out of bed but remained at home about a week. He then returned to heavy work, but was not so strong as he had been before the injury.

After the accident he lost control of the bladder, so that when he

<sup>6</sup> Jour. Nerv. and Ment. Dis., 1907, p. 665.

<sup>7</sup> Semaine méd., December 26, 1906, p. 616.

coughed or exerted himself the urine would escape. This condition became worse gradually until he had no control of the bladder, and was obliged to wear a urinal. Sexual desire was not weakened, but the dribbling of the urine prevented the sexual act. The rectal sphincter functionated feebly and a call to stool was urgent. His gait and station were good. The lower limbs were well developed, but the man felt weaker than before the accident. The left side of the scrotum, the left side of the perineum, and the left buttock near the anus had fully normal sensation to touch and pin prick; whereas the right side of the scrotum except the upper outer portion, the right buttock in a small area near the anus, and to a less degree the right side of the perineum, showed diminished sensation to touch and pin prick. The right side of the penis also was less sensitive than the left side. The sensation of the testicles was normal. The patellar reflexes were prompt but the Achilles reflexes were slight. Babinski's sign was not present. The upper part of the body was not affected. The lesion seemed to be in the lower sacral roots, and may have been confined to one side because of the unilaterality of the disturbance of sensation in the supply of these roots. This unilaterality seemed to indicate that the lesion was not in the conus. The cause of the symptoms was probably stretching of the lower sacral roots of one side by excessive straining in lifting a heavy weight while bending forward.

## GELATINOID CARCINOMA (MORBUS GELATINOSUS) OF THE PERITONEUM.<sup>1</sup>

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THE special interest in this case is concerned with several points: (1) It is an example of ascites existing over a long period and requiring a large number of tapings. (2) The problem of diagnosis. (3) The character of the peritoneal fluid. (4) The interpretation of the autopsy findings.

The history is as follows: G. B., a colored man, aged thirty-eight years, a butcher by occupation, was admitted to the Jefferson Hospital first on February 21, 1911.

<sup>1</sup> Read at the meeting of the Association of American Physicians, May, 1915.

*Family History.* His father died at fifty-eight years from asthma, his mother at sixty years, the cause not being known; he has six brothers and sisters living and well; one died from an accident and one from typhoid fever. There is no history of tuberculosis.

*Personal History.* Measles, mumps, and chicken-pox in childhood were the only infectious diseases. There is no history of cough or shortness of breath. The appetite and digestion have been good. There was no history of any illness suggestive of appendicitis. There is no note of any urinary trouble. He had a gonococcus infection at the age of eighteen, but gave no history of a luetic infection. The patient had used only small amounts of alcohol.

*Present Illness.* In the summer of 1910 the patient noticed there was some enlargement of the abdomen. This occurred without any pain or disturbance of the stomach or bowels. The distention did not last long and the patient states that it disappeared entirely. In January, 1911, the swelling of the abdomen returned and increased gradually until he was admitted to the hospital. There had been no pain, and the patient complained only of discomfort when coughing or stooping over. He had some shortness of breath on severe exertion, but worked until five days before admission. Otherwise he had been in good condition and did not complain of any gastric or intestinal trouble.

*Examination.* The patient was well nourished. There was no definite jaundice. The lungs showed dulness at both bases and the heart was displaced upward. These were both regarded as being due to the pressure from the abdomen. The abdomen showed very marked enlargement and the usual signs of ascites. The liver and spleen could not be felt. There was no edema of the scrotum and very slight edema of the legs. The blood count showed hemoglobin, 68 per cent.; reds, 4,900,000; leukocytes, 7400. The urine had a specific gravity which varied from 1.015 to 1.030, and generally contained a small amount of albumin, but was otherwise negative. The abdomen was tapped and about nine liters of fluid removed. This presented the usual appearance of ascitic fluid, and was not peculiar in any way. The specific gravity was 1.030, and there was a considerable amount of albumin. The majority of the contained cells were lymphocytes. After the tapping the fluid reaccumulated for a time and then diminished. He was discharged with evidence of some fluid in the abdomen, but in good general condition. The picture at this time was apparently that of cirrhosis of the liver with ascites.

During the following three years the patient was admitted to the hospital seventeen different times. It does not seem necessary to mention these in detail, and only the important points are given, which, for convenience, may be put under separate headings.

*General Condition.* The patient's general health remained extremely good. The only complaint which he made on each return to the hospital was of the abdominal distention. It was only on his last admission, March 4, 1914, that any change was noted. He had then lost weight and was suffering from frequent vomiting, which apparently prevented his getting sufficient nourishment.

*Abdominal Condition.* This was much the same on each admission. The degree of distention varied somewhat, but was always quite marked. The usual physical signs of ascites were always present. There were no signs suggesting any disease of the gall-bladder, appendix, or cecum. Examination of the rectum did not show any abnormality.

*Abdominal Tapping.* Up to the time of his last admission he had been tapped fifty-eight times. On forty-six occasions fluid was obtained, the amount of which varied from 2500 c.c. to 10,560 c.c. During a period of about three years from the onset, he was tapped nine times and the fluid had always the same character as noted on the first occasion. On the tenth tapping (May 22, 1913) a different state of affairs was found, which will be referred to later. One curious point was that on several occasions he was much better after an attempted tapping which was not successful. On two admissions there was no successful tapping, but the patient was discharged very much improved and with the distention lessened.

The patient, naturally, became an authority on the methods of being tapped, and always graded the different house officers under whose care he came, according to their ability to tap. He emphasized two characteristics which the trocar should have, namely, that it should be sharp and of large size.

On May 22, 1913, there was a distinct change in the material obtained by tapping. On this occasion a number of gelatinous masses escaped with the ascitic fluid. This was about three years after the onset and about one year before death. These gelatinous bodies varied in size from about the size of a grain of wheat to an ordinary pea; occasionally larger masses were obtained. Their appearance was gelatinous and in some ways rather suggested boiled tapioca grains. The larger masses that were obtained had much the same appearance. Occasionally the trocar was completely blocked with these, but, as a rule, they did not interfere materially with the tapping. About a month later, as tapping was again required, it was thought well to do an exploration, and a small incision was made in the abdominal wall. A large quantity of fluid was obtained and the same gelatinous colloid-like material. The opening was not large enough to permit of any extensive investigation of the abdomen, but nothing abnormal in any of this viscera was noted through the small incision. The fluid at this

time showed 83 per cent. of small lymphocytes, 11 per cent. cells with large nuclei, and the remainder polynuclear cells and others difficult to classify.

The problem of diagnosis was a most interesting one. The patient had chronic ascites, but his general condition was excellent and there was no jaundice. In August, 1913, the abdomen was markedly distended, with definite evidence of ascites, but this was not extreme. For the first time enlargement of the liver was found and the edge of the left lobe was felt in the midline 3 cm. above the navel. It seemed quite distinctly irregular. It was not possible to feel the edge of the right lobe with certainty. The spleen was considerably enlarged and readily felt below the costal margin. In view of the long duration of the ascites, the fact that it had come and gone, the patient's excellent general condition, and the enlargement of the left lobe of the liver and spleen, the question of syphilis of the liver had to be considered. However, the Wassermann reaction was always negative and no signs of syphilis were to be found unless the abdominal condition was due to it. Still it seemed worth while to let the patient have some potassium iodide, and it was begun at this time. We never felt sure that it made any difference, although the patient claimed that after taking it the fluid accumulated much more slowly. During this admission the patient was tapped a number of times, the fluid always containing the same gelatinous masses.

Examination of the cells in the ascitic fluid showed considerable variation in the percentage of lymphocytes at various tapplings, and also in the occurrence of eosinophiles. At this time (August, 1913) it was not possible to be certain that the right lobe of the liver was enlarged, but a little later this was definitely made out, and in January, 1914, the edge in the right nipple line was felt 10 cm. below the costal margin. The enlargement of the left lobe previously noted was still present. So far as we could determine there had been a definite increase in the size of the right lobe. In view of the fact that he had been taking potassium iodide quite steadily for some months, this was strongly against the possibility of the enlargement of the liver being due to lues. The last admission was on March 4, 1914. By this time his general condition showed marked change, shortness of breath and edema were more marked, and he had been much troubled by vomiting. Examination of the stomach contents did not show anything of special interest except that no free hydrochloric was obtained. The blood showed only a moderate secondary anemia; the differential count was normal. The obstinate constipation which he had on admission was soon replaced by persistent diarrhea. We tested the length of time which it took for material to pass through the bowel and found that this was usually about four or five hours. When the condition of the intestines was seen at autopsy this seemed very remarkable.

The difficulty of tapping increased so that sometimes it was necessary to tap in several places before we could obtain any fluid. There were eleven successful tapplings on the last admission. At times he complained of severe abdominal pain, but did not show any marked tenderness. It was not possible to feel either the liver or the spleen at this time. About two weeks before death a number of *nodular masses* were felt in the abdomen. These were evidently in the peritoneal cavity, felt quite superficial, were very hard, and quite freely movable. They varied in size from a diameter of about half an inch to perhaps one and a half inches. They were felt in different places on different days. The vomiting and diarrhea continued until death on May 7, 1914.

The main facts may be summarized as follows: A male, aged forty-one years, with chronic ascites for four years and fifty-seven successful tapplings. For three years the fluid showed no peculiar features and then gelatinous colloid-like material appeared and was present for a year until death. During the greater part of this time the patient's general condition was excellent. The liver and spleen showed enlargement at one time and later became reduced in size. Shortly before death many hard, rounded, movable masses were felt in the abdomen. There was intractable diarrhea for the last few weeks of life.

The gelatinoid material was studied in the laboratory of our colleague, Professor Hawk. It was a mucin-like substance, much like the material known as serosa mucin. It contained 11.5 per cent. of nitrogen and 0.8 per cent. of sulphur.

The question arises as to the course of events, and it must be confessed that the autopsy did not throw much light on this. For three years the patient had ascites regarded as due to cirrhosis of the liver. But cirrhosis of the liver without some other condition does not, as a rule, permit of repeated tapplings over such a long period, for ascites is usually a terminal event in pure cirrhosis. With the appearance of the gelatinoid material in the ascitic fluid the question arose whether the process had been of a malignant character from the onset. If so it must have been extremely mild. The presence of ascitic fluid with the characteristics of that found in cirrhosis of the liver has been noted for some time before the appearance of signs suggesting a malignant process. Thus in the case reported by Pye-Smith, during a period of ten months the patient was tapped seven times and the usual fluid of ascites secondary to cirrhosis was found. On the next tapping cells were found which suggested colloid carcinoma. This was the celebrated case in which tapping was done 299 times. Death occurred after a duration of nearly nine years, and at autopsy a papillomatous tumor of each ovary was found. The peritoneum was thickened and covered with secondary papillomata.

Another obscure point was that three months after the first

finding of gelatinoid material the liver and spleen were found to be enlarged and six months later the enlargement was still more marked. Subsequently the liver decreased in size, and before death the liver and spleen could not be felt. There does not seem to be any explanation for the increase in the size of the liver and spleen. The enlargement was not secondary to circulatory failure. The size of the liver at autopsy was proof that we had not been mistaken in the belief that the enlargement had disappeared. In the absence of cirrhosis it seems probable that the decrease in size of the liver was due to the marked increase in the thickness of the capsule. It may be suggested that the enlargement did not actually exist but the liver was very easily felt after tapping and the increase in size occurred under observation. The position of the upper limit of dulness did not change.

**PATHOLOGICAL REPORT.**<sup>2</sup> The body is that of a poorly nourished adult colored male. *Rigor mortis* is present but easily broken up. Pupils equal and contracted. Slight edema of both ankles. Abdomen greatly distended and tense. Subcutaneous fat is very scanty. Abdominal and thoracic musculature is pale red and greatly atrophied.

As matters of special interest pertain to the abdomen a brief survey only will be given to the other findings:

Left pleura slightly thickened; cavity contains a few cubic centimeters of slightly turbid, yellowish fluid. Between the lobes of the left lung, situated immediately under the pleura, are several elevated grayish areas, 5 to 10 mm. in diameter, which on section show a lobular arrangement, the alveoli containing a grayish transparent gelatinoid substance. Although the lung appears small it crepitates throughout except a narrow stratum at the base; the lower lobe is also somewhat congested.

Right pleura is dry; the serosa slightly thickened, especially over the base. On the pleural surface of the diaphragm are a few grayish gelatinous bosses and granulations; the largest of the former measures a little over 1 cm. in diameter; the fine granulations may be exudative or neoplastic, of which one cannot be sure. The nodules in the muscular portion of the diaphragm have raised the serosa, which is still, apparently, intact. Except for a few areas of partial collapse and considerable congestion, a large part of which is clearly hypostatic and associated with some edema, the lung is not the seat of any noteworthy abnormality. In neither lung was any secondary growth observed. No metastasis in the mediastinal lymph nodes or other tissue except the subpleural growths already mentioned.

Pericardium uninvolved. Heart is displaced upward and slightly

<sup>2</sup> Section and preliminary examination made by Dr. E. D. Funk, demonstrator of morbid anatomy, upon whose protocol the following is in part based. Much of the general description deemed immaterial to this presentation is omitted.



to left. No important lesion. There are a few negligible sclerotic areas in aorta and larger branches.

Except for a mild patchy fibrosis the kidneys are normal. No gross change in adrenals. No noteworthy lesion in bladder or genitalia.

Permission to examine the central nervous system was not obtained.

*Abdomen and Contents.* As the incision approaches the abdominal cavity it is noted that the parietal peritoneum is thickened, at points almost leathery, and in such areas resists incision. When the abdomen is widely opened the almost universal presence of a gelatinoid material is observed. It has accumulated particularly in the pelvis, lumbar regions, right and left, and between the stomach and liver. About 2500 c.c. were removed; all that would adhere to visceral and parietal peritoneum was left in position; it was thought that formalin fixation would secure it in place, but to a slight degree only was this result attained. The greatly thickened parietal peritoneum was dissected loose from the muscles on each side and posteriorly, the diaphragm incised along its attachment to the parietes, and the entire mass removed for fixation and further study. The following data were obtained from examination of the fresh specimen, and later, after formalin fixation, by such dissection as was permissible without destroying the specimen (see Fig. 1).

The upper border of the specimen is formed by the diaphragm, which on the inferior surface is intimately attached to every viscus with which it comes in contact. The attachments to the liver and spleen are particularly firm. The intestines, including the colon, and the stomach are closely packed in the median line and matted together by adhesions, many of which are so firm that the enclosed viscus tears before the adhesion yields. Nothing that could be certainly identified as omentum remains distinguishable in the mass. Between the stomach and liver is a cavity holding more than a liter of gelatinoid substance. This has displaced the stomach downward and rather behind the colon to which it is firmly attached. The transverse colon is greatly dilated, the dilatations being most marked near the hepatic and splenic flexures. To this part of the colon is also attached the small intestine, heaped in an indistinguishable mass. With a long brain knife the anterior portion was cut away, exposing the opened convolutions of the intestines beneath. With difficulty these were separated above, as shown in the illustration, to permit palpation of the pancreas, which does not appear changed. The caput coli is greatly dilated and the wall slightly thickened. The outer aspect of the caput coli and a part of the descending colon and sigmoid are attached to the parietal peritoneum. The ascending colon passes mesially almost to the midline behind the small intestine and ascends tortuously to the hepatic flexure. A similar mesial displacement of the descending

colon is also present. Apparently these displacements are due to pressure of gelatinous masses occupying the lateral aspect and



FIG. 1. Contents of abdomen. Anterior aspect. Carcinoma of peritoneum. Upper margin formed by liver and attached diaphragm. Just below liver, between that organ and stomach, cavity containing gelatinoid material; cavities to right and left and also pelvis contained similar material. Every part of serosa in contact with any other surface is adherent. Some of these adhesions have been broken up. Intestines are rigid and stand open on section. Note nodules on abdominal wall, especially to lower right. For further description see text.

lumbar region of the abdomen. The area of the gall-bladder and pylorus is occupied by a dense fibroid mass containing many small cavities filled with gelatinoid material.

Incision through 5 cm. of this mass opens the gall-bladder; the cavity is 9 cm. long and irregularly compressed with a maximum breadth of 3 cm. It is filled with bile-stained gelatinoid material somewhat thinner than much of that in the peritoneum, but may be scooped out as a semisolid mass, dark greenish-yellow in color. The mucosa is smooth. The bile ducts were not dissected.

The liver is small, capsule greatly thickened; adhesions practically universal to all surfaces. Several incisions disclosed no secondary growth. Microscopically the cells are granular and shrunk, with a slight increase in fibrous tissue, most notable beneath the capsule.

The appendix was found buried in a mass of adhesions, and though not fully dissected is about the thickness of the little finger and admits a probe 8 cm. The connection with the cecum is closed and the base of the appendix bulges into the cecum as an ovoidal boss 2.2 cm. in diameter. On incision it is found to contain the same gelatinoid material as that present in the abdominal cavity and gall-bladder. The obvious thickening is around the appendix rather than of the appendix; the musculature and mucosa are not thicker than normal, if anything, at least in areas, they appear thin. The great and irregular thickening of the parietal peritoneum is well shown in the illustration. Just below the right lobe of the liver the thickening extends through the peritoneum and into the aponeurosis of the muscle. Neither macroscopically nor microscopically is the wasted muscle found involved. The inner surface of the parietal peritoneum is covered with loosely attached gelatinoid or colloid material; relatively little of this substance is shown in the illustration. There are also, at many points, on the parietal peritoneum and on the adhesions binding the viscera, numerous nodules varying in size from 2 to 3 mm. to 4.5 cm. In the illustration two of these are well shown at the lower right on the parietal peritoneum, and on the mass of adherent intestines in the median line near the lower border. Masses of exactly the same type are also free in the peritoneal cavity; several of these were removed, attached on a frame, and photographed (Fig. 2). Incised in the fresh condition they were found to possess outer capsules 1 to 3 mm. in thickness, and to contain soft gelatinoid material which flowed from the cut surfaces with about the same consistency as thick egg albumen. Fixed in formalin they retained their contour and bore incision without loss of contents. Several of those shown in Fig. 2 exhibit the essential morphology. Running in from the capsule are numerous fine delicate trabeculae without regularity of arrangement, forming a sort of a reticulum, in the meshes of which is contained the gelatinoid substance. Numerous histological sections show these to be composed of imperfectly developed fibrous tissue containing a few round cells, an occasional leukocyte, and homogeneous staining gelatinoid material. In

none of the sections was any epithelium encountered. It was evidently these structures that could be palpated through the abdominal wall during life. Several were still loosely attached

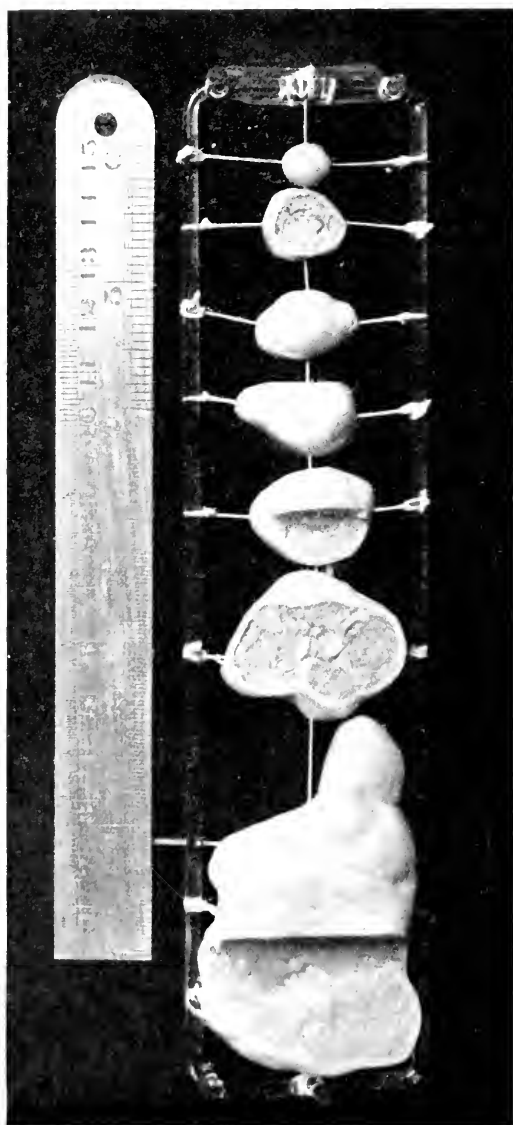


FIG. 2. Nodules from peritoneum. Many of these, of practically every size, the largest 5 cm. in diameter, were free in the belly cavity or loosely attached, often by a thin filament only, to the abdominal wall. Those shown were all free. For further description see text.

and apparently about to separate from the wall or the visceral mass. Examination of one of the attached masses seemed to indicate that they arise from condensation of the gelatinoid material



FIG. 3.—Section of parietes. Abdominal wall immediately below liver mass. Photomicrograph. A, muscle of abdominal wall; B to C, muscle fascia, extra-peritoneal tissue, and peritoneum in single thick layer of dense fibrous tissue, at points separated by interstitial edema; C to D, stratum in which neoplastic growth is at points demonstrable. Just above leader from C, stratum of columnar epithelial cells, most of which are of the tall palisade type. Note that just beneath epithelium edema is marked; D, and above, reticulum partly enclosing spaces containing homogeneous gelatinoid material; E, space clearly outside peritoneum; a few disappearing epithelial cells along upper margin, others below; space filled with gelatinoid substance; square outlined in centre is shown under higher magnification in Fig. 4.

which later becomes edematous, the characteristic cellular elements disappearing. Their development is entirely internal to the structure that was thought to occupy the position of the normal peritoneum. Ssobolew observed similar bodies.

*Morbid Histology.* Sections of the organs are for the most part without interest. Several of the gelatinoid masses removed at operations and others obtained postmortem, were fixed and stained by appropriate methods without disclosing any cellular element upon which a histological diagnosis could be based. Similar disappointing results were obtained from numerous examinations made of parts removed from several areas in the parietal peritoneum and from the thickened masses of adhesions. Most of these showed an exceedingly edematous fibrous reticulum obviously in various stages of formation. The general character of the histological appearance may be gathered from a close study of the photomicrograph shown in Fig. 3, which includes the edge of the abdominal muscle below; above is the denser fascia, the peritoneum showing the neoplastic involvement, and at the top the reticulum surrounding irregular communicating spaces containing the homogeneous, almost cell-free, gelatinoid substance. It will be observed that the latter contains a scanty cellular detritus and nothing upon which a histological diagnosis as to the character of the process could be based. However, in the examination of a large number of sections numerous pictures similar to that shown in the centre of the field were encountered. Note the papillary growth projecting upward surmounted by tall columnar epithelium the cell nuclei of which are margined immediately at the bases of the cells. The higher magnification of this same area is shown in Figure 4. Many of the epithelial cells are of the chalice type. The connective tissue immediately underlying the cells is, in practically every instance, obviously edematous, and apparently when the edema reaches a certain stage the cell disintegration begins and continues until the epithelium entirely disappears.

The morphology and chemical reactions of these cells are identical with those observed in the palisade epithelium commonly found lining the varieties of ovarian cysts with which this disease is so frequently associated; no one who has examined the structure has any doubt as to the epithelial origin. Identical appearances in growths obviously connected with the appendix have been reported.

In the many sections examined structures possessing the same general characters as those described have been found only occasionally. Such growths, however, have been observed in the extraperitoneal fascia and in the diaphragm immediately beneath both peritoneum and pleura.

The almost universal involvement of every structure in the abdominal cavity in this case, and the absence of any conclusive dominance in one particular area renders impossible an unassailable statement as to the origin of the process. Those who believe strongly in its appendicular relation will lay stress on the fact that the appendix is involved. An examination of Fig. 1 must

impress the observer with the fact that the gall-bladder area is conspicuously affected. At this point the colon, gall-bladder, intestine, pyloric complement of stomach, diaphragm, and abdominal parietes are implicated. If finding gelatinoid material in the cavity of a viscus could be taken as proof of origin in that organ, there would be some ground for the statement that in our patient the process might here have arisen in the gall-bladder. Had the pri-



FIG. 4.—Small central area from Fig. 3 more highly magnified. Photomicrograph. In centre papillary growth covered with tall columnar epithelium; many cells are of the chalice type. Part of another papillary growth is shown at left. To right note regressing epithelium; edema at base of papillary mass and beneath palisade epithelium.

mary lesion been in the appendix one would not have expected so extensive an involvement of the upper abdomen. Of course, without more detailed section than has been made it has been impossible to exclude the stomach, duodenum or pancreas, or indeed for that matter almost any part of the intra-abdominal alimentary canal. It is quite certain that such a tumor might have originated in a diverticulum. In the absence of later and more exact information concerning the nature of these growths the condition would

probably have been regarded as a primary neoplasm of the peritoneum; this possibility, we think, may be excluded.

Of special interest is a consideration of the nature of the process concerning which many views have been held. Pean, forty-five years ago, applied the term gelatinous disease of the peritoneum, fully recognizing and admitting the vagueness of the term. In

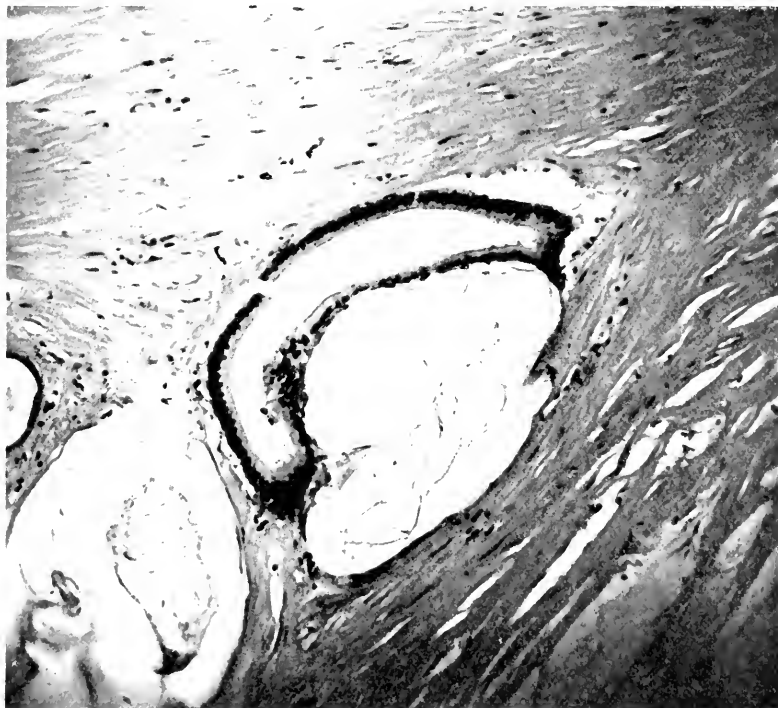


FIG. 5. Section from fibrogelatinoid area in gall-bladder region. Photomicrograph. Typical epithelial lined space showing regression of epithelium and edematous gelatinoid substance arising beneath the epithelial cells; over this substance the epithelium is disappearing. Below and to left (left lower corner) is a mass of gelatinoid substance containing two regressing epithelial cells. It has not been possible with certainty to determine the origin of this gelatinoid substance. Just below centre of left margin part of vessel in stratum of fibrous tissue. A few fibroblasts and an occasional leucocyte may be recognized.

some form no doubt this was what Virchow called colloid cancer and to which has also been applied the terms mucoid cancer, gelatinous ascites, and carcinomatous ascites. Werth, in 1884, introduced the name pseudomyxoma, to which there are many objections, but which unfortunately has been widely adopted, and under which name most of the cases are recorded. We believe the process is neoplastic and essentially cancerous, but would manifest no par-



ticular preference between the terms colloid, mucoid, muciparous, or gelatinoid carcinoma, if anything, inclining toward the last. The designation "*maladie gelatineuse*" is not inappropriate. Failure to recognize the carcinomatous nature of the process rests upon the fact that endless search or exceptional good fortune in any particular case may be necessary to locate the areas of definitely cancerous morphology. The fact that invasion extends through the peritoneum into the muscle fascia, through the diaphragm from serosa to serosa, with the formation of subpleural nodules, the nodules between the lobes of the lung, and other evidences seem to us difficult of explanation except on the assumption that the process is potentially malignant.

The universality of the retrograde changes in the epithelium, not commonly encountered in cancer, is due to some influence which our study has failed fully to disclose. Apparently the proliferating epithelium is encountering some antagonistic influence that is constantly breaking it down. The epitheliolytic agent seems to be of humoral origin. No evidence of phagocytosis, no noteworthy leukocytic infiltration, no giant cells, are present, but an edema, in which the epithelium seems to undergo disintegration and solution without leaving behind the usual detritus incident to chromatin fragmentation commonly observed in the presence of a necrosis and cell disintegration. In Fig. 5 it can be noted that beneath the epithelium on the under side of the space lined by cylindric cells there is a collection of edematous gelatinoid material over which the epithelial cells are manifesting retrograde changes. In a space below and to the left the epithelium has almost completely disappeared, and this retrogressive change on the part of the epithelial cells is manifest in almost every location where they are found. The influence that brings it about seems to come after the cell is growing or in some instances after the cell is fully grown, suggesting that the growth of the cell is necessary for its appearance. Following conventional usage it would be easy to suggest a name for such a hypothetical body; at the risk of being prosaic we forego this.

It is well established in this class of cases that complete removal of early manifestations may be curative, and that admittedly incomplete excision of advanced lesions may be followed by long intervals before recurrence takes place and in some instances apparent recovery. Such cases have been recorded by Lejars, Trotter, Neumann, Eden and others. In one of Lejars's cases the tumor disappeared. In Eden's patient gelatinous disease due to an ovarian tumor was present at operation done "several months" after appearance of symptoms; the ovary and a large part but not all of the jelly were removed; three months later the patient was well. Two years and four months after the first operation the other ovary and appendix were found involved and removed.

Nearly two years later the patient was reported well. According to Lejars, lesions of ovarian origin are more malignant than those arising in the appendix.

Destructibility of cells composing or derived from malignant tumors has been established by numerous observers, and more recently has been especially investigated by Iwasaki. Twenty years ago Goldmann suspected the presence of some protecting body. Hodenpyl's results obtained by injecting ascitic fluid derived from a patient with cancer aroused hopes that have not materialized. Our case and many in the literature more than suggest the existence of some such body and of tissue and humoral potentialities that we may in the future find some way to mobilize. The peritoneum may be able to produce such an agent. Bland-Sutton says "large numbers of cancer cells which are shed into the abdominal cavity perish, for the peritoneum exercises defending or prophylactic power against such marauders." We know that tissues engaged in processes essentially protective in nature suffer, often are almost destroyed when the fight is lost; note the lymph-nodal changes in many infections, such as plague and tuberculosis, the liver necroses in infections and intoxications and consider the destroyed omentum in some of these peritoneal neoplasms. Possibly that organ of inconclusively-established function may be playing a part of which we know nothing. According to Theilhaber there are on record 200 cases of cancer spontaneously cured. Coley's results in sarcoma cannot be ignored. The problem is to determine by what mechanism the result is attained.

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## THE CLINICAL RELATIONS OF GRAVITY, POSTURE AND CIRCULATION.

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THE vascular mechanism is everywhere in a state of "tone" by which its capacity is actively reduced. Were the physiological tone to be released the capacity of the blood channels in the splanchnic area alone would be sufficient to contain all the blood and the circulation would come to an end in the erect posture because no fluid could reach the heart.

This tonicity of the vascular bed is what keeps the blood from stagnating in the capacious reservoirs of the abdomen under the influence of gravitation. It is essentially a vital phenomenon. There is a distinction between the regulating mechanisms for the preservation of tone in the arteries as contrasted with the veins of the splanchnic system, but an essential adjunct to the proper function of the veins is the mechanical support afforded by the normal tension of the abdominal wall.

Physiologists have supplied us with fundamental data for the apprehension of the hydrostatic disorders of the circulation.

The experiments of Leonard Hill<sup>1</sup> are especially rich in significance. Hill secured animals (dog, cat, monkey) upon a board which could be rotated in a vertical plane. The animal could then be readily turned from the horizontal to either a feet-down or feet-up posture. Both arterial and venous blood-pressure were graphically recorded throughout the experiments.

It was found in the four-footed animal that the carotid blood-pressure always fell in the feet-down posture, and rose in the feet-up posture, as compared with the horizontal. The fall of arterial pressure in the first case was due to the accumulation of blood in the splanchnic veins and a correspondingly lessened inflow into the heart; the higher arterial pressure in the last case depended on a plethora resulting from excessive emptying of the abdominal veins.

In a small dog changing from the feet-down to the feet-up posture caused the carotid pressure to vary from 16 mm. Hg. below to the same amount above the normal. In certain of the animals, especially in the monkey, the hydrostatic effects of changed posture were compensated and the carotid pressure remained normal; in the feet-down posture there was active splanchnic vasoconstriction and in the feet-up posture the reverse. Chloroform anesthesia tended to disable the mechanism of compensation. Under chloroform narcosis the splanchnic vasomotor mechanism was paralyzed and in the feet-down posture the blood from the general circulation would gradually collect and stagnate in the splanchnic veins, the heart become empty and ceased to beat. If in such a case it was attempted to revive a heart by resorting to the head-down posture the inrush of blood would overdilate and paralyze the weakened organ. Chloroform prevents the normal contractile reaction of the heart. A bandage tied around the abdomen or pressure applied with the hands readily compensated for the fall of blood-pressure in the feet-down posture by preventing the accumulation of blood in the veins. Sudden removal of pressure upon the abdomen in the feet-down position could drain the heart and kill the animal.

In general, according to Hill, any influence which weakens the splanchnic vasomotor mechanism or, the writer would add, that lowers the contractile tone of the abdominal wall, magnifies proportionately the postural effects of gravity on the circulation.

These postural changes in the carotid blood-pressure are of profound importance in determining the blood-pressure and circulation within the brain. On account of the rigidity of the skull the brain remains, according to Hill, practically at a constant volume. Its vessels are never, while the cranium is intact, drained of blood, but the circulation may stagnate in the brain of feet-down animals. When in such a posture a trephine hole is made in the

<sup>1</sup> Jour. Physiol., 1895, xviii, 15.

skull the brain at once collapses, becomes drained of blood, and the animal quickly dies. Hill had an opportunity to verify on a man with a trephine hole in his skull the intracranial pressure changes dependent on posture. He calls attention to the danger in elevating the head of a patient with a defect in the skull when the vasomotor mechanism is incompetent.

Bayliss, Hill, and Gullard<sup>2</sup> declare that "the brain has no direct vasomotor mechanism, but its blood supply can be controlled indirectly by the vasomotor centre acting on the splanchnic area." They find that "the intracranial pressure in all physiological conditions remains the same as the cerebral venous pressure. The intracranial pressure is wholly circulatory in origin and may vary with the circulatory from zero to 50 to 60 mm. Hg. The functions of the brain matter continue with the varying conditions of pressure." Under "physiological conditions a rise of arterial pressure accelerates the flow of blood through the brain and a fall slackens it. . . . The rise of arterial pressure that occurs in pathological conditions of increased intracranial pressure is not protective but tends to increase the extent of the cerebral anemia. The right direction of treatment therefore in such conditions is to lower the blood-pressure." Though strong evidence is furnished by other experimenters that the vessels of the brain are not devoid of vasomotor fibers the main contentions of the authors quoted hold good.

Hill and Barnard<sup>3</sup> dwell especially on the application of these data in the human subject. "In a man six feet high the hydrostatic pressure of a column of blood reaching from the vertex to the sole of the feet equals about 140 mm. Hg., and from the vertex to the middle of the abdomen about 50 mm. Hg. . . . The splanchnic vasomotor mechanism is by itself amply sufficient to compensate for the hydrostatic effect of gravity. . . . In man a condition of deficient vasomotor tone combined with an atonic condition of the abdominal wall or patulous abdomen must in the erect posture lead to a deficient circulation and anemia of the brain."

Surgical shock furnishes the most startling exhibition of the vital disaster attending circulation failure in the intact vascular circuit. Passing the extensive literature dealing with the pathology of this condition the writer will assume as proved that view according to which acute traumatic shock has its origin neither in heart failure nor vasomotor failure. This conclusion in no way surrenders the notion that vasomotor failure may have an important etiological bearing on the conditions with which this paper deals.

Basing his views on animal experimentation, Yandell Henderson<sup>4</sup> announces the theory that shock, both surgical and toxic, depends upon the accumulation of blood within the large veins of

<sup>2</sup> Jour. Physiol., 1895, xviii, 334.

*Ibid.*, 1897, xxi, 323.

<sup>4</sup> Amer. Jour. Physiol., 1910, xxvii, 152.

the abdomen, from which reservoir it fails to flow into the heart. The animal behaves as if bled to death within his own vessels. According to Henderson the large abdominal veins are normally maintained in a state of tone not by vasomotor nerves, but through an intrinsic venopressor mechanism whose efficiency essentially depends upon the tension of  $\text{CO}_2$  and of the acid-alkali balance in the fluids of the body. This conception of the chemical and osmotic regulation of the venopressor mechanism of the splanchnic area suggests that any departure from healthy metabolism may cause virtual dilatation of the abdominal reservoir and lead to stagnation of blood within it when the erect posture is assumed.

From the purely clinical point of view, T. C. Janeway<sup>5</sup> some years ago clearly pointed out that those familiar catastrophes which we were wont to designate as "heart failure" are, for the most part, not heart failures at all but vascular failures put into effect by the postural drainage of the blood into the "abdominal reservoir." While in the normal man or animal the bloodless heart might easily be revived by restoring the vital current, in the toxemic, shocked, or anesthetized subject it could easily happen that a brief period of bloodlessness would fatally reduce cardiac irritability.

Hill<sup>6</sup> has shown that efforts to restore the circulation under shock conditions by the feet-up posture are prone to result in paralysis of the heart by overdilatation. Clinicians are familiar with the hazards involved to patients with debilitated hearts when the bowels are moved in the sitting posture; especially, probably, is this the case during states of flux. The special danger lies, presumably, in a diminished splanchnic tone on these occasions.

A most important corollary to all these teachings is the expression of the unity of the circulatory system. There is no rational study of heart disease by itself. The efficiency of the heart depends as intimately upon the efficiency of the bloodvessels, their nerves, and of tissue metabolism and osmosis as upon the integrity of its own structures, and all must be taken into account by the philosophic physician.

The mechanical conditions surrounding the circulation in the brain and in the abdomen are in significant contrast. In the former the rigidity of the skull keeps the organ relatively full of blood even with a zero of arterial pressure. Under such a condition there must be exerted upon the brain tissues molecular tensions which may have profound physiological importance, but of whose mode of action we are wholly ignorant. In the abdomen, on the other hand, the bloodvessels find less support, perhaps, than in any other situation. The physiological integrity of the splanchnic vasomotor system and of the musculature of the abdominal wall form the chief or only extraneous limitations to expansion of the

<sup>5</sup> New York Med. Jour., 1907, lxxxv, 193.

<sup>6</sup> Loc. cit.

great "abdominal reservoir." Numberless facts support the conclusion that the vascular bed of the abdomen is the great variable in the irrigating system of the body, now contracting, now expanding, to meet the needs of the tissue soil. Simple as might seem the relations of the physical factors which determine pressure within the abdomen, nowhere is more obvious the futility of the deductive method in physiological investigation. Emerson<sup>7</sup> summarized the literature on the nature and conditions of intra-abdominal pressure up to 1911, and was not able to establish any consensus of opinion from the authorities. By some the intra-abdominal pressure is held to be positive, above that of the atmosphere, by others negative, below it.

It is rather generally admitted that the pressure is positive or varies with respiratory movement, increasing with inspiration and decreasing with expiration, and that it becomes negative in subjects having pendulous abdominal walls. Emerson himself, on the basis of animal experiments, concludes that the normal pressure within the abdomen is slightly positive, due to the coördination of numerous physiological factors. The pressure slightly rises or falls with descent or ascent of the diaphragm. Excessive diminution of pressure induced by loss of tone in the abdominal wall, or, on the other hand, untoward increase of pressure, as in meteorism, each reduces more or less critically the efficiency of respiration and circulation.

Burton-Opitz<sup>8</sup> demonstrated experimentally the profound alterations in the extra-abdominal circulation attending comparatively slight changes in intra-abdominal pressure. The tendency of positive pressure, as might have been expected, was to force blood out of the abdominal veins and impede the inflow into them. The resultant effect was to increase the amount of blood circulating through the head and diminish it in the lower extremities.

An extensive and practical study of the abdominal circulation in its clinical relations has been made by Oliver.<sup>9</sup> This author points out again that though the hydrostatic effects of postural change are much more manifest on the veins than on the arteries, still arterial pressures are largely subject to gravitation. In the standing position the blood-pressure in the arteries of the head may be but one-half that in the feet, and the latter pressure may fall one-half in the horizontal posture. He has no hesitation in saying that in the normal subject the arterial pressure in the erect position, sitting or standing, is higher than in the recumbent. That is, splanchnic vasomotor tone normally overcompensates the hydrostatic effect of gravity. Fatigue, disease, laxness of the

<sup>7</sup> Arch. Int. Med., 1911, vii, 754.

<sup>8</sup> Amer. Jour. Physiol., 1914, xxxvi, 66; Arch. f. d. ges. Physiol., 1908, cxxi, 156; *ibid.*, 1908, cxxiv, 469.

<sup>9</sup> Blood and Blood-pressure, 1901.

abdominal wall, or any influence which lowers the vasomotor tone or reduces the external support of the abdominal vessels tends to relatively raise the arterial pressure in the recumbent posture. The reason for this seems obviously to consist in the gravitation of blood to the abdominal veins in the erect and corresponding delivery of it to the general circulation in the horizontal posture.

Oliver states that "overloading of the splanchnic veins, from diminution or loss of tone in the arterioles which feed them, is a common, if not an invariable, fact in all forms of debility. . . . In splanchnic states the normal postural variation of the radial caliber is reversed."

Oliver's method of estimating the amount of splanchnic venous stasis is simple and effective. With the subject in the horizontal position the arterial pressure is measured in an arm, then a maximum weight of twenty-eight pounds, a bag of shot, is equally distributed over the abdomen. Excess of blood in the abdominal veins is thus forced toward the heart and the arterial pressure rises proportionately. Observations made before breakfast, when the vascular tone is high, show little or no rise of arterial pressure with abdominal compression. But for thirty minutes after a meal a weight applied to the abdomen may send the arterial pressure up 17 or 20 mm. Hg. Observations repeated at intervals afterward show less and less elevation of pressure with compression. In the healthy subject at rest, abdominal compression might raise the arterial pressure 18 mm. Hg. After vigorous but not exhausting exercise compression of the abdomen had no effect on arterial pressure, owing to excessive dilatation of the systemic vascular bed. But when exercise was continued to fatigue, loss of splanchnic vasomotor tone was evidenced by rise of arterial pressure when weight was applied to the abdomen.

It is important to understand definitely the nature of the interdependence between the tensions of the abdominal wall and the splanchnic veins. If, as Emerson<sup>10</sup> and others have concluded, the intra-abdominal pressure becomes constantly negative when the abdominal wall is patulous, we must recognize therein a steady force tending to aspirate the blood into the thin-walled veins of the cavity. The commonly associated condition of visceroptosis probably acts in the erect posture to still further lower the pressure when the weight of the organs directly stretches the containing wall. In brief, positive intra-abdominal pressure tends to empty and negative pressure to fill the abdominal veins.

The general conception of the pathological significance of intra-abdominal pressures has been the theme of much fugitive medical literature within the past decade or more. The one idea at the root

<sup>10</sup> *Loc. cit.*



of most of this writing has been derived from palpation of the abdominal wall. Ptosis of the abdominal organs thus disclosed has been held responsible for a long category of pathological symptoms, and the manufacture of devices for correction of the defect employs a host of artisans from whom we can hardly demand an appreciation of etiology. It is not intended here to make a sweeping denial of the pathological importance of visceroptosis, but to point out that, in the majority of cases, clinicians in attributing symptoms to postural dislocation of the abdominal organs have probably mistaken the shadow for the substance.

The foregoing imperfect sketch of the literature dealing with the postural relations of the abdominal circulation almost reduces to platitude the deduction that loss of tone by the splanchnic vasomotor system and the abdominal wall must result, in the erect posture, in anemia of the brain and oligemia of the general circulation.

The various debilities which may initiate such a failure of tone are, in turn, intensified by its effects, and the vicious circle thus established constantly contracts at the expense of normal function.

The muscles of the abdominal wall are said to be innervated from the respiratory centre. Much remains to be discovered concerning their coördination with the vasomotor system and their relations to the acid-alkali balance of the blood. It is open to suspicion that the teleological idea behind the abdominal rigidity attending peritoneal inflammation is not more to limit painful friction between surfaces than to reduce blood flow within them. The comforting effect of the ice-bag may depend upon the same result.

Dr. C. D. Mosher<sup>11</sup> describes the great relief experienced by her patients with congestive dysmenorrhea when they lay with hips elevated and pressed firmly over the uterus and breathed deeply. This sort of manipulation is well adapted to relieve pelvic congestion.

My own impression of the clinical importance of postural abdominal stasis was not formulated in advance, but was built up by induction from the observations carried on through many years. The facts under consideration are familiar to every clinician; their relation to symptomatology and the indicated *rationale* of treatment seem so obvious that special exposition might appear superfluous, yet somehow it is clear that medical practitioners in great part either fail to understand the data involved in this situation or misapprehend their significance.

In the normal subject the fall of carotid blood-pressure, which tends to occur on changing from the recumbent to the erect posture, leads to stimulation of the splanchnic vasomotor centre; at the same time the tension of the muscles of the abdominal wall is apparently

<sup>11</sup> Jour. Am. Med. Assn., 1914, lxii, 1297.

increased, as is evidenced by the difficulty found in making a satisfactory palpatory examination of the abdomen with the patient upright. In these ways the hydrostatic pressure tending to surcharge the splanchnic veins may be even overcompensated, so that, with the venous outflow from the brain accelerated by gravity and the arterial inflow kept high by elevation of systemic arterial pressure, the nourishment of the brain may be expected to flourish best in the erect posture.<sup>12</sup>

The important aid given in the standing posture to the flow of blood through the lower extremities by the tension and contraction of great masses of skeletal muscles need not be here considered. Suffice it to say, we seem justified in concluding that when the recumbent posture is assumed, at once all the nervous and muscular activities which were engaged in hydrostatic compensation come to rest and gravitation no longer impedes the return of the blood from the abdomen to the general circulation.

When we turn from the healthy to the debilitated individual we must expect to witness the preponderance of gravity effects proportional to the weakening of the physiological powers which had held it in compensation. Now, in the erect posture, the blood actually stagnates to a degree in the splanchnic veins at the expense of the systemic circulation and the blood-pressure in the brachial artery falls. Changing to the recumbent posture the surplus fluid overflows into the heart and the brachial blood-pressure rises. Simple as the problem may appear, investigators differ in their statements of the facts as to the influence of posture on the arterial blood-pressure in the normal human subject. Oliver<sup>13</sup> states emphatically that in the normal subject the pressure in the radial artery is higher in the erect than in the recumbent posture; he finds the arterial pressure in the sitting posture to average about 10 mm. Hg. more than in the supine. Stephens,<sup>14</sup> on the contrary, in a study of 22 cases, presumably healthy young men, found the systolic blood-pressure invariably higher in the recumbent position. His average postural pressures in mm. Hg. were: standing, 130.8; sitting, 131.7; supine, 150.4. The photographs of his experimental arrangements indicate that the arm in which the pressure was measured was raised considerably above the heart in the erect and supported below it in the supine position.

Erlanger and Hooker,<sup>15</sup> in a careful study of two young men, found that on changing from the recumbent to the erect posture there might be either a slight rise or fall of maximal pressure in the brachial artery, but the characteristic effect of the change was a diminution in the pulse pressure in the erect posture, caused by a rise in the minimal blood-pressure. "If on standing the minimum

<sup>12</sup> *Vide infra* Erlanger and Hooker.

<sup>13</sup> *Loc. cit.*

<sup>14</sup> *Jour. Am. Med. Assn.*, 1904, xliii, 955.

<sup>15</sup> *Johns Hopkins Hosp. Rep.*, 1904, xii, 145.

pressure rises but little the maximum will fall more; but if the minimum pressure is decidedly increased the maximum may rise." On changing from the recumbent to the standing posture they found a rise of minimal (and mean) pressure, as a rule; a diminution of pulse-pressure, an increase of pulse rate. The reverse changes occurred when, after standing, the recumbent posture is assumed. The pressures found in the sitting posture approached those of the recumbent much nearer than those of the standing posture. When the external temperature was elevated they found the minimal pressure to be lower and the pulse-pressure to diminish less on standing.

They say, "The circulation in the brain is, if anything, improved in the sitting and especially in the standing postures." As will be seen, it is exactly the pathological reverse of this cerebral circulation efficiency to which I attribute the symptoms which suggested this investigation. The complexity of the subject has been sufficiently demonstrated to warn us against deductive reasoning which must be based on premises some of which are unknown. Nevertheless, it is proper to consider the directions in which functional efficiency may be expected to become impaired under definite anatomical inadequacies.

Physiologists have shown that experimental reduction of the blood flow to the brain excites the vasomotor centres, especially of the splanchnic areas, with the obvious effort to increase the intracranial blood flow. We can hardly doubt that in a person whose blood gravitates abnormally into the splanchnic veins there is produced a virtual anemia of the brain capable of setting up a functional disability which may be manifested in a wide variety of ways. Patients belonging to the affected class often complain of great muscular weakness. They are apt to develop the general functional incapacity or perversion which we are prone to group under the head of "neurasthenia." Headache and dizziness in the erect posture are characteristic symptoms. It is as if the nervous centres protested against an inefficient effort, as in eye-strain.

Perhaps the most dramatic case among my records is that of an active business man, about fifty years of age, who had gradually developed annoying headache and dizziness for which the neurologist and aurist failed to effectually account. The symptoms manifested themselves only in the erect posture, disappearing when the subject lay down. The patient presented a dazed appearance. His heart was dilated and the abdomen somewhat protuberant. His blood-pressures were: sitting, 104-62; recumbent, 109-69. There was no obvious arteriosclerosis. The patient was made to stand up and hold a pillow over his abdomen. Standing just behind him with my arms around his body, strong pressure was brought to bear on the pillow over the lower abdomen. At once he declared

himself free from headache and dizziness, which symptoms immediately returned on relaxing the pressure. The experiment was repeated several times with the same result. An abdominal belt was prescribed and was worn during the daytime for about six weeks, with complete relief of symptoms. It is interesting to note that for several months after removal of the belt the patient remained normal. Headache and dizziness then occasionally returned, to be relieved by application of the belt, which was resorted to rather unwillingly because of the local discomfort it gave. Great reduction in the cardiac dilatation accompanied the general improvement.

In many of the cases which seem to belong to this category I had no opportunity to make definite blood-pressure observations, but have depended on the therapeutic test for diagnosis. Thus a dentist, aged about forty-five years, whose large practice necessitated his standing by his chair throughout the day, complained of continued exhaustion which compelled him to take frequent vacations. When he adopted an abdominal belt exerting firm pressure over the lower half of his abdomen he experienced a return of vigor which enabled him to do his work with comparative ease. In the group of complaining, more or less healthy-looking women in whom it is so difficult to localize the pathological condition, and which the physician commonly characterizes as "neurasthenic," measures taken to support the abdominal circulation, often seem to give better results than any other, whether or not there is evidence of enteroptosis. A patient, aged sixty years, who frequently feels an approach of faintness when driving his motor car, has learned that he can quickly restore himself to normal by a series of vigorous contractions of the abdominal muscles. The effect, of course, is to unload the abdominal circulation as by massage.

The one physical sign which seems to be indicative of general, and especially of intracranial, hydrostatic circulation deficiency is to be found in the postural changes of the blood-pressures.

Study of a relatively small number of healthy subjects leads me to agree with the majority of observers in this field, that in the normal person in the erect, at least in the sitting, posture the blood-pressures are higher than when recumbent.

When I find the blood-pressures, especially the maximal, higher in the recumbent than in the sitting posture I conclude there is physiological weakness either of the splanchnic vasomotor system, of the abdominal wall or both and that potential cerebral anemia and vasomotor overstrain are consequences in the erect posture.

In studying a series of cases it becomes obvious that there is no strict parallelism between the acuteness of the symptoms and the difference in the postural heights of blood-pressure. It is probable that, as illustrated in the first case recorded above, the urgency of the symptoms is due to nervous efforts to compensate for hydrostatic failure of the circulation.

In persons employed in earning their living at more or less sedentary occupations, whom through years it has been difficult to keep keyed up to their work, I have learned to expect a higher recumbent blood-pressure. When there is cardiac degeneration a considerable excess in the blood-pressure when recumbent is, in my experience, a bad prognostic sign.

Having been led by such experiences as have been detailed to suspect that splanchnic stasis is a potent cause of many of the disabilities, such as weakness, headache, dizziness, for which the physician is consulted and an important factor in many specific disorders, it seemed to me desirable to study the blood-pressures in their postural relations, with a view to establishing a rational basis of treatment.

My observations were made with a Pilling sphygmomanometer. With the patient sitting the broad cuff was applied around the bare arm, the forearm resting upon a table. At least three estimations of maximal and minimal pressures were made by the auscultatory method. Without detaching the cuff the patient was then made to lie on a couch and the observations were repeated, care being taken to preserve the relative position of cuff to heart.

The diastolic pressure was assumed to correspond with the beginning of the "fourth phase" of sound from the relaxing artery.

In carrying out such work with people physically below par it is astonishing how variable are the individual sound phases both as to their occurrence and intensity.

If these observations were to be repeated I would choose the beginning of the fifth phase, or the cessation of sound, as the point of minimal pressure.

A curious manifestation, apparently significant of functional nervous instability, is not infrequently witnessed in a rapid change in the height of maximal arterial pressure in consecutive observations under constant conditions. The minimal pressure takes an insignificant part in these fluctuations. They seem to be due to subconscious mental perturbations. Nervous women with hypertension at and beyond the menopause are especially apt to show the vasomotor instability. In these cases, in a series of consecutive observations the maximal pressure is prone to be considerably higher in the early than in the late measurements. It is significant that these wide differences in maximal pressures, amounting to 10 mm. Hg. or more, seem to occur only in the sitting posture, in which the vasomotor effort must be most active.

Goodman and Howell<sup>16</sup> have performed a useful service in calling attention to the relation which they claim to exist between the duration of the sound phases and cardiac efficiency. The duration of each sound phase is indicated by the number of millimeters fall which the mercurial column suffers within that phase and the ratio

<sup>16</sup> AMER. JOUR. MED. SCI., 1911, cxlii, 334.

which this bears to the pulse pressure is determined. Increase in the second and third phases is held to be a sign of cardiac strength; of the first and fourth of cardiac weakness; the ratio of the two is then easily determined. Swan<sup>17</sup> used the method in the study of a considerable number of clinical subjects and believes it to give a valuable index of the ratio of cardiac strength to cardiac weakness.

The subject is mentioned here because my observations indicate that postural changes which redistribute the blood have marked influence on the existence and prominence of the sound phases and, as already said, circulation efficiency is measured by the integration of conditions throughout the vascular tract.

Very few of the patients to be considered were the subjects of cardiac or vascular disease. None was confined to bed. A few had long ceased to need medical care.

The subjects have been divided into two groups. The first group is composed of those whose systolic blood-pressure in the sitting posture is equal to or greater than that in the recumbent posture. The cases number 26 (9 males and 17 females) with ages varying from eight to fifty-five years. The second group is composed of those whose systolic blood-pressure is greatest in the recumbent posture. The cases number 40 (17 males and 23 females) with ages ranging from eleven to seventy-seven years. The averages of the blood-pressures under all conditions are represented in the accompanying table:

AVERAGE BLOOD-PRESSURES IN MM. HG.

	Posture.	Maximum.	Minimum.	P. P.
I. 26 cases	Sitting	123	77	46
	Supine	120	73	47
II. 40 cases	Sitting	116	71	45
	Supine	122	72	50

Occasionally a patient is found who on one occasion will fall within this and on another into that group. It is not expedient to dwell upon the individual clinical characteristics of the two sets of subjects, but it is interesting to observe that though nearly all were sufficiently below par to seek medical advice, there is a rather lower average physiological grade in those in the second group having the higher recumbent maximal blood-pressure.

This conception is of decided practical value, for included in the second group is a number of persons whose main dyscrasia, such as tendency to acidosis, slight tendency to cure in pulmonary tuberculosis, neurasthenia, might easily depend upon a remedial weakness of the circulation. Perhaps the most significant pressure change in Group II is the rise of the average minimal pressure in the recumbent posture. According to Erlanger and Hooker, there is normally a decided fall in minimal pressure in the recumbent as

<sup>17</sup> Internat. Clinics, 1911, iv, 130.

compared with the erect posture. While in all of Group II the maximal pressure was higher in the recumbent than in the erect posture the minimal pressure was higher in the recumbent posture in 23 cases and lower in 15.

The lowering of minimal pressure with a rise in the maximal on assuming the recumbent posture does not support the conclusions of Pilcher<sup>18</sup> who found, in general, that under all conditions modifying maximal pressure the minimal pressure changed in the same direction if in different degree.

Inherent difficulties impair accuracy in the estimation of the minimal blood-pressure, especially in such debilitated persons as were the subjects of these observations; one or more of the sound phases may be absent or drop out in a change of posture. In such a case the terminal sound was taken to mark the minimal pressure.

My own data seem to indicate that the more normal the subject the more likely is the maximal blood-pressure to fall in changing from the sitting to the recumbent posture, and still more likely is the minimal pressure to fall. Consequently, as suggested by Elanger and Hooker,<sup>19</sup> increase in the pulse pressure in the recumbent as compared with the erect posture is a mark of physiological harmony. Treatment for splanchnic stasis has frequently been instituted on account of clinical symptoms alone; when relief has been experienced by these patients an examination of their postural blood-pressures has always shown them to be included in my second group, that in which the systolic pressure is higher in the reclining posture. The relations of splanchnic stasis to intoxications from the digestive tract seems well worth investigation, but the subject appears to have received little or no attention.

A study of the table from which my averages are made in connection with histories of the patients suggests very definitely that a similar table constructed with adequate care from a large number of subjects would be of prognostic value in the estimation of life insurance risks.

My efficient intern on medical service at the Denver County Hospital, W. K. Hobart, made a prolonged study of the postural blood-pressures in a dozen cases, including 5 with bronchial asthma and chronic bronchitis and 1 convalescent each from lobar pneumonia and typhoid fever. In the pneumonia case, as convalescence became established, the minimal blood-pressure fell markedly in the recumbent posture and the pulse pressure increased correspondingly. In a case of severe chronic nephritis and arteriosclerosis the systolic blood-pressure was usually considerably higher sitting than lying, but the pulse-pressure was reversed from the normal, being higher in the sitting posture. In the, mostly very severe, cases of bronchial asthma all pressures were very variable; four of the

<sup>18</sup> Amer. Jour. Physiol., 1915, xxxviii, 209.

<sup>19</sup> *Loc. cit.*

patients showed at times an extraordinary fall in the pulse-pressure sitting, due to rise in the diastolic pressure. Mere laxness of the abdominal wall, which of itself must tend to splanchnic stasis in the erect posture, may be overcompensated, probably through splanchnic vasomotor spasm, in a most unexpected way. But in such cases I have found that while the maximal blood-pressure might, imitating the normal condition, be higher in the sitting than in the recumbent posture, the value of the minimal pressure, and of the pulse-pressure, would depart more or less widely from the postural variations of health. The general conclusion from the observations is that the postural relations of the blood-pressures, especially as manifested in the fluctuations of the pulse-pressure, are an important index to the state of physiological efficiency.

**TREATMENT OF ABDOMINAL BLOOD STASIS.** Oliver,<sup>20</sup> in his monograph states the problem in the treatment of splanchnic stasis to be "to widen the bed of the skeletal arteries, to unload the splanchnic veins, and to tone the splanchnic arterioles." Tension and respiratory and resistance exercises and cycling are advised as especially adapted to gently unload the abdominal veins into the systemic arteries. It is important that each exertion should be followed by a period of rest in the recumbent position. Baths with alternating temperatures, conjoined with percussion and massage which cause dilatation of the systemic vessels have a favorable effect. Oliver points out that the physiological determination of blood to the abdominal viscera during digestion makes it especially advisable that the recumbent position be assumed after each meal. The subject should lie down for an hour at such times, and it is advised that during the latter half of this period a weight of ten to fifteen pounds, conveniently in the form of a bag of shot, be distributed over the abdomen.

These measures seem reasonable, and to them should be added exercises especially adapted to strengthening the abdominal muscles, such as raising the legs or the trunk from the recumbent posture, contraction of the abdominal muscles against resistance, etc.

The rowing machine would seem to be particularly fitted to strengthen the weakened functions. But while our ideal must be correct physiological defects by physiological means, and to strive for it, in medical practice we adopt such measures as relieve morbid symptoms in the quickest way. I know of nothing which so nearly fulfils this purpose in splanchnic stasis as artificial support applied over the lower abdomen.

From the numerous devices heralded for this purpose it is difficult to find one which is at once comfortable to the patient and effective in achieving results. The problem seems easier in the case of women who can wear a corset, laced in front, by which abdominal



pressure can be regulated to a nicety without interference with respiratory movement. The fixture—belt, band, or corset—should be adapted to the individual who wears it, and should be regarded as a makeshift during the endeavor to reestablish correct physiological relations.

**SUMMARY AND CONCLUSIONS.** This contribution is a plea for the view that splanchnic stasis is not a pathological curiosity, but that it is potentially present, and may be the starting-point for vicious circles of derangement in every case of general functional weakness.

It has been shown that in the erect posture the blood would largely gravitate into the splanchnic veins were it not for the reaction of physiological mechanisms of which the splanchnic vasomotor apparatus and the muscles of the abdominal wall are the chief factors. Laxness of the abdominal wall, probably leads, in the erect posture, to the establishment of a negative pressure within the abdomen, which it is a prime object of treatment to correct.

It is pointed out that depletion of the intracranial blood current must follow insufficient compensation of the hydrostatic pressure involved in the erect posture. Virtual anemia of the brain leading to a multiplicity of disorders, not the least of which is probably vasomotor overstrain, is the natural sequence. It is probable that excess of blood-pressure in the recumbent as compared with the erect posture is a trustworthy index of splanchnic stasis.

No attempt has been made here to exploit the possible influence of splanchnic stasis on the oxygenating power of the lungs or their resistance toward infection or on the metabolism of the abdominal viscera and intoxications arising therefrom.

## THE FASTING TREATMENT OF DIABETES MELLITUS, WITH SPECIAL REFERENCE TO ACIDOSIS.<sup>1</sup>

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SINCE its inception by Rollo the dietetic treatment of diabetes mellitus has had as its object the attainment of the aglycosuric state. To attain this state, carbohydrate was withdrawn from the diet; this was done, but never quite satisfactorily, because with-

<sup>1</sup> Read before the New York Academy of Medicine, December 21, 1915.

drawal of carbohydrate from the diet, it was believed, precipitated acidosis. And because it was supposed to precipitate acidosis, prolonged fasting was considered inadvisable, although it was recognized that the occasional fast days of Naunyn diminish acidosis. This procedure was not followed, because it was thought that "fats burn in the fuel of carbohydrate." The spirit of this phrase has dominated the modern treatment of acidosis. The doctrine that overfeeding with fat is harmless and even beneficial in increasing weight and strength and that carbohydrate feeding is required to avert threatening coma has done much to retard the progress of the treatment of diabetes. In point of fact the excess of fat in diet disposes the patient to acidosis; the excess of carbohydrate to glycosuria. Now it has been found that both features of the disease—glycosuria and acidosis—must be recognized and controlled. Both can be influenced by diet; both can be influenced by fasting. In order that treatment by these means may be properly applied it is necessary to understand the effect of diet and fasting upon both glycosuria and acidosis. As far as glycosuria is concerned a few days of complete fast may render the patient sugar-free and a subsequent restriction of diet may suffice to maintain him in this state; but the control of acidosis is more difficult and involves a comprehensive understanding of the problem of acidosis in general. It is, indeed, the presence or absence of this condition which is now regarded as the dominant factor in determining the course of treatment. In view of this fact the present paper is limited to a discussion of this phase of the subject.

**Acidosis.** By acidosis is meant a decreased alkaline reserve of the blood rather than an increased acidity. An accumulation of acids sufficient to create an acid reaction in the blood and tissues is incompatible with life. The alkalinity of the blood is maintained chiefly by the amount of bicarbonate it contains. This amount may be estimated indirectly in terms of carbon-dioxide tension in the alveolar air, directly by the power of the blood plasma to combine with carbon dioxide. If acids accumulate in the blood and tissues sufficient to neutralize a portion of the bicarbonate there present, they reduce the alkaline reserve of the blood and tissues below normal. When this occurs it is accompanied by a diminution in the power of the blood plasma to combine with carbon dioxide and consequently causes a parallel diminution in the tension of alveolar carbon dioxide. This condition is known as acidosis, although an acid reaction of the blood never occurs unless *in extremis*. Acidosis, therefore, may be defined as a lessened bicarbonate reserve in the blood and tissues. It may be caused either by an overproduction of acid bodies in metabolism or by a lessened excretion of these substances.

The need of a method to determine the amount of acid bodies in the medium where accumulation takes place is obvious. That

medium is the blood. Tests of the urine are valuable only for the excretory phase of acidosis. They may be misleading in that they give no index of the accumulation of these substances in the blood due to overproduction or to faulty elimination.

*Methods for Determining Acidosis.* Until recently urinary tests alone have been used as indices of acidosis. These tests have included qualitative tests for acetone and diacetic acid; quantitative determinations of the acetone bodies, of ammonia, and of total acidity. So long as excretion keeps pace with acid formation, tests of this nature are satisfactory; but when excretion of acid substances is imperfect, as may occur in diabetes, the elimination cannot keep pace with production. Therefore urinary tests may not reveal the degree of acidosis present. During the past thirteen years Beddard, Pembrey, and Spriggs<sup>2</sup> have published a series of papers on the amount of carbon dioxide in the blood, the urine, and the alveolar air as criteria of acidosis in diabetes. Since 1913<sup>3</sup> they have abandoned blood analyses in favor of determinations of the alveolar carbon dioxide, because their studies led them to believe that "estimations of alveolar carbon dioxide by Haldane's method are at present the best guide for the prognosis and treatment of diabetes." The alveolar carbon dioxide, being an indirect measure of the bicarbonate content of the blood, is significant, but in abandoning examination of the blood the English investigators have substituted an indirect measure of acidosis for a direct one. The indirect method, namely, the alveolar carbon-dioxide determination, is an accurate indicator of the reserve bicarbonate of the blood only when respiration and circulation behave in an entirely normal manner both as regards mechanical efficiency and nervous control. The fact that Beddard, Pembrey, and Spriggs gave preference to the indirect alveolar-air method, despite its possible inaccuracies, may be attributed to the lack of a satisfactory technic for blood analysis.

**VAN SLYKE'S METHOD FOR DETERMINING THE BICARBONATE CONTENT OF THE BLOOD.** During the present year a direct and exact method has been introduced by Van Slyke<sup>4</sup> for determining the bicarbonate content of the blood as measured by the power of the blood plasma to combine with carbon dioxide. This method not only eliminates the error of measuring the blood alkalinity by an indirect method but has the added advantages of simplicity, rapidity, and accuracy. It avoids, furthermore, the error due to personal factors. Van Slyke's apparatus consists of a glass pipette in which the plasma is acidified and the bound carbon dioxide is set free. The volume of gas may be read directly from the scale on the instrument or may be expressed in terms of volume per cent. carbon dioxide in the blood by reference to tables with corrections

<sup>2</sup> *Lancet*, 1903, i, 1366.

<sup>3</sup> *Jour. Physiol.*, 1913, xlviii, x.

<sup>4</sup> Method to be published in the *Journal of Biological Chemistry* in the near future.

for temperature and barometric pressure. By a further simple calculation the figure obtained may be translated into terms of alveolar carbon dioxide tension.

This method affords a simple clinical means for determining the bicarbonate content of the blood. The blood estimation in conjunction with urinary findings gives an index of the production and elimination of acid bodies, a knowledge of both of which is essential to an interpretation of the clinical picture. In those instances in which an analysis of the blood cannot be made, valuable information may be obtained by determinations of the alveolar air.

**FRIDERICIA'S METHOD FOR DETERMINING ALVEOLAR CARBON DIOXIDE.** In 1914 Fridericia<sup>5</sup> published a modification of an already well-known method for analysis of the alveolar carbon dioxide so simple and so easily applied to clinical use that it merits a brief description. A glass tube with stop-cocks is so arranged that 100 c.c. of expired air can be readily collected for analysis. The sample of air is shaken with an alkaline solution within the glass chamber and all the carbonic acid is absorbed by the alkali so that the amount of gas absorbed may be read directly in percentage from a scale marked on the tube.

**SYMPTOMS OF ACIDOSIS.** The symptoms due to acidosis vary. They range from the mere irritability, mental torpor, and lessened physical alertness of chronic low-grade acidosis through the hyperpnea, drowsiness, and headache of high-grade intoxication to the nausea and vomiting which presages the onset of diabetic coma. A careful study of the manner in which 22 cases have behaved while fasting has suggested that they may be divided into groups of four definite types. Any given case may react differently to fasting on different occasions. This classification is based on the study of acid production and elimination [as determined by blood bicarbonate content and urinary acid excretion].

Group I is composed of cases which maintain a normal bicarbonate reserve of the blood throughout the course of their treatment.

In Group II are placed the cases which recover, while fasting, from acid intoxication, sometimes so severe as to verge on coma.

Group III consists of those cases which show a low-grade acidosis as indicated by a subnormal bicarbonate reserve and heightened ammonia excretion.

Group IV includes those cases which develop acidosis while fasting, though previously no evidence of acid intoxication existed.

1. The cases which show no diminution of bicarbonate in the blood during the fasting period are milder diabetics. They are made aglycosuric easily by a few days of fasting and they do not develop untoward symptoms or clinical signs of acidosis during

<sup>5</sup> Berl. klin. Wehnschr., 1914, ii, 1268.



more or less extreme drowsiness. Fasting is followed by amelioration of all these symptoms. The sodium bicarbonate reserve in the blood rises and generally becomes normal on the third or fourth day, although the urine may not show a lessening in its reaction for ketone bodies until later in the treatment. In these cases the fast should be continued until aglycosuria results. (Chart II.) The patients are then treated by the method in use in this hospital<sup>6</sup> until they remain permanently aglycosuric.

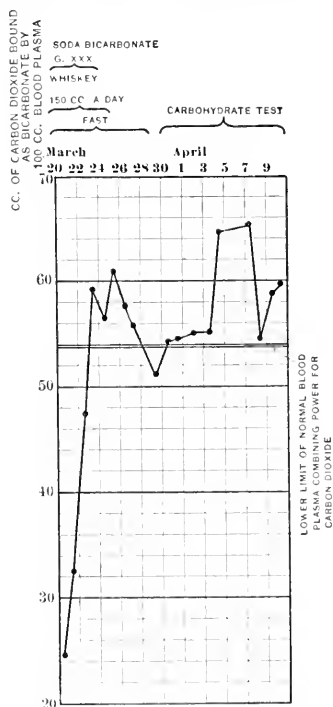


CHART II.—Patient, aged seventeen years. High glycosuria and ketonuria from March 19 to 26. The power of the blood plasma for combining with carbon dioxide rose to normal during the fast, and remained normal after.

III. The cases which show a low-grade chronic acidosis before, during, and after their fast comprise the most difficult group to treat successfully. (Chart III.) One may suspect that a patient belongs in this group from some or all of the following signs:

1. Chronicity of the diabetic symptoms.
2. Lessened mental acumen.
3. Lessened physical alertness.
4. Tendency to a low-grade but continuous glycosuria.

<sup>6</sup> The details of the general and dietetic management employed will be described in a paper to be published later.

5. Low carbohydrate tolerance.
6. A certain degree of obesity.
7. Persistent lipemia.
8. Lessened sodium bicarbonate reserve in the blood
9. A slight but extremely obstinate ketonuria.

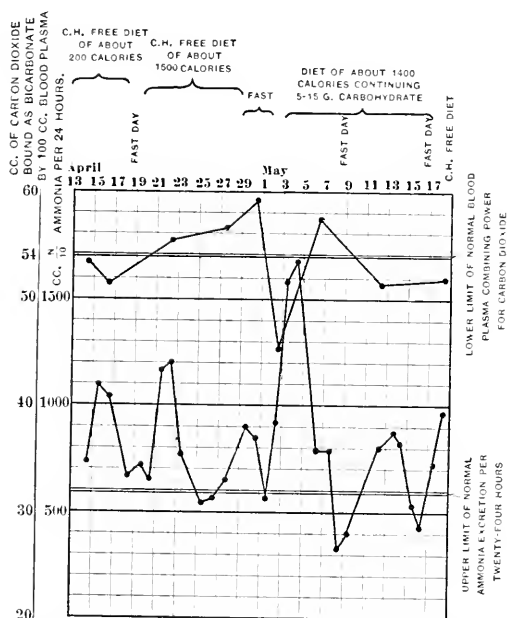


CHART III.—Patient, aged eighteen years. The patient was observed for fifteen months. This chart is taken from the middle of this period. During the first months of treatment the degree of acidosis was continually higher. At this period and thereafter the acidosis was less marked. Prolonged fasting caused a slight decrease of the power of her blood plasma to combine with carbon dioxide. This increase in the acidosis is not characteristic for the group but is a reaction which may be expected in fasting persons. The ammonia excretion, always high, increased still further to meet the demand for regulation. (These phenomena will be published in detail in another paper.)

These characteristics, as well as the readiness with which the acidosis is increased by fat feeding, suggest that the faulty metabolism of carbohydrate is complicated by difficulty in the complete combustion of fats. The fasting period required to clear up glycosuria may be long. During this period the urine may not become negative in its reaction for ketone bodies, and the bicarbonate content of the blood may maintain its subnormal level. When the aglycosuric condition is reached the patient may still show a low carbohydrate tolerance, rarely more than 60 to 100 grams of carbohydrate in the form of green vegetables alone, and may tolerate only from 0 to 15 grams when allowed a mixed diet of low caloric value (15 to 25 calories per kilogram of body weight).

An excessive supply of fat, even of body fat, together with a low carbohydrate tolerance, apparently plays an important part in the symptomatology of patients in this group, and it is toward the correction of these conditions that treatment should be directed. A continuous subcaloric diet with fast days interpolated twice a week rapidly rids the patient of excessive body fat, while the lowered total caloric intake allows of a greater amount of carbohydrate in the diet without the appearance of glycosuria. Even though the

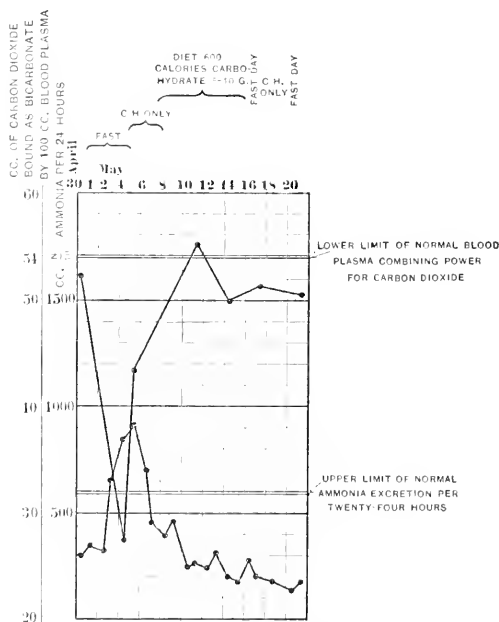


CHART IV.—Patient, aged twelve years. On admission she had a slight glycosuria and slight ketonuria. During the fast the ketonuria intensified while the glycosuria disappeared, and they both have been absent since. During the fast the degree of acidosis increased to a dangerous extent. The ammonia excretion, though increased, was inadequate. The fast was terminated and acidosis disappeared as measured by the power of the blood plasma to combine with carbon dioxide—the excretion of ammonia and ketone bodies. Two subsequent fasts were attended by no untoward return of these phenomena. (The lower normal level for the power of the blood to combine with carbon dioxide in a child, aged twelve years, should be placed between 50 or 52 instead of at 54.)

loss of weight may appear excessive it is not to be feared. In some instances as much as one-fifth of the body weight has been sacrificed before the clinical, blood, and urinary evidences of acid intoxication have disappeared. Lipemia generally disappears rapidly with the loss of body fat. The patient becomes tolerant of more carbohydrate, the urine loses its reaction for ketone bodies, and the blood gradually rises in its bicarbonate content. Not infrequently months of treatment are necessary to obtain good results in these patients. But persistence, no matter how discouraging treatment



may appear, is almost always rewarded. So far it has been possible to discharge all of these cases on a diet sufficient for their comfort and usefulness and no tendency to a spontaneous return of the former symptoms has been observed.

The cases comprising Group IV are those which develop signs and symptoms of acidosis during the fasting period, though previously no evidence of an acid intoxication may have been shown. (Chart IV.) The hidden danger of impending acidosis may be masked by their apparent state of good health and nutrition. Glycosuria sometimes appears to be the only abnormal factor in an otherwise satisfactory status. Urinary tests may show either a heavy or a negative reaction for ketone bodies. On the second or third day of the fast vague symptoms with irritability may appear. This condition is at first attributed to hunger, but on the following day the symptoms become intensified and nausea may develop or drowsiness supervene. Then the significance of the situation is recognizable. Should fasting be continued still longer, hyperpnea or vomiting, which usually indicates the onset of coma, may occur. During the development of these symptoms, even though the urine may sometimes gradually become clear of glycosuria and the ketone reaction remain slight or only mildly positive, the analysis of the bicarbonate of the blood shows an increasing tendency toward the danger zone. This group emphasizes the necessity of an early recognition of the onset of acidosis and illustrates the advantage of a clinical method which aids in its detection. In these instances acidosis may be manifested when fasting is instituted. The daily analyses of the blood indicate the degree of acidosis and provide the opportunity to control the dangers to which such patients are subjected during the fasting period. A progressive downward tendency of the bicarbonate content of the blood offers a clear-cut therapeutic indication. In these cases fasting should be discontinued. If such a patient is put on a low protein-fat diet the symptoms of acid intoxication may disappear after the first feeding and the bicarbonate content of the blood continues to rise until a normal level is reached and danger of coma is past. After several days of such diet a second fast has always, thus far, been well tolerated and has cleared up the glycosuria successfully.

Twenty-two diabetics have been studied with reference to the effect of prolonged fasting on acidosis. They may be divided into the groups just described, according to their response to fasting as follows:

Group.	Number of cases.	Percentage of cases.
I . . . . .	10	45.4
II . . . . .	2	9.1
III . . . . .	8	36.4
IV . . . . .	2	9.1
Total . . . . .	22	100.0

The ten cases (45.4 per cent.) comprising Group I were benefited by the fasting method. They were rendered aglycosuric very rapidly and their stay in the hospital was very materially shortened.

The effect of fasting in the cases of Group II (9.1 per cent. of the series), which show evidence of being in a state of profound acid intoxication, is especially striking. These cases improve, within twenty-four hours, in such a manner that they may be considered out of danger of coma, although they were admitted to the hospital bordering on this state. The two cases cited received sodium bicarbonate (30 grams per diem until the blood bicarbonate reached normal) together with whisky (150 c.c. per diem divided into ten doses). Recently we have treated two additional cases in Group II; they fasted without receiving either bicarbonate of soda or whisky and improved in an equally satisfactory manner. The radical departure in this from previous methods consists in not giving carbohydrate to ward off coma. Certain of our results show that the feeding of carbohydrate in such cases may actually precipitate coma.

The patients comprising Group III (36.4 per cent. of the cases studied) were freed from a chronic low-grade acidosis by prolonged fasting and subsequent continued subcaloric feeding. The temporary undernutrition is not harmful, and temporary loss which is encountered is rapidly made good by improvement. Without the temporary delay, subsequent improvement is often unattainable.

The remaining cases—Group IV—(9.1 per cent. of the series, are those in which serious or fatal results are possible from prolonged fasting if the fasting is not controlled and suitable warning is not heeded. The clinical symptoms alone may not afford sufficient indication of the threatening danger, but the use of the methods described renders fasting safe. Under suitable control, therefore, the fasting treatment can be conducted with safety even in cases of this type.

SUMMARY. The following conclusions may be briefly summarized thus:

I. The object of the fasting treatment of diabetes mellitus is to render the patient permanently free not only from glycosuria but also from acidosis.

II. The term acidosis signifies not an actual acid reaction, but an accumulation of acid bodies in the blood and tissues sufficient to neutralize enough of the bicarbonate there present to reduce the alkaline reserve below normal.

III. Urinary tests for acidosis are often misleading in that they are indicative merely of the excretion of acid bodies and are not a true index of their accumulation. An analysis of the blood bicarbonate as determined by the power of the plasma to combine with carbonic acid, on the other hand, offers an accurate measure of the accumulation of fixed acids and gives a true index of the degree of acidosis present.

IV. For convenience of description the diabetics above described were classified into four groups. This classification is based on the type of response to prolonged fasting as indicated by the degree of blood alkalinity.

V. When the degree of acidosis present is determined daily by the method described, experience so far indicates that all cases of diabetes may be treated by the fasting method safely and with benefit.

## THE EAR-TESTS OF BARANY IN LOCATING CEREBELLAR AND OTHER ENCEPHALIC LESIONS.<sup>1</sup>

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THE importance to the aural surgeon of the Barany tests is generally known, and they have even been overworked in leading to needless operations upon the labyrinth; but in the broader aspects of diagnosis we have probably made only a beginning, and it is to this side of the matter that we would claim attention, particularly the attention of the otologist, who alone can rightly make some of these investigations, since the neurologist and the general surgeon rarely have the needed otological training: and the otologist, for that matter, must renew or enlarge his neurology if he is to progress accurately in this complex field. Yet time for successful intervention in many intracranial morbid conditions is usually short and may not permit of any elaborate coöperative study by a group of specialists—success will be highest when competent head and hand can be united in one person, as we have seen in the low mortality of lateral sinus thrombosis when operated on by the skilled aural surgeon.

With so good a leader as Barany in this modern advance, progress has been rapid and generally sure; yet errors have crept in at many points and obtained temporary currency; and only the combined critical study, tested and corrected by the crucial touchstone of operation or autopsy, can convert the findings from empiric gropings into scientific data leading on to new conquests. For this the large hospitals offer fine opportunities, and we have been very fortunate in Philadelphia to have been able to utilize these to a notable extent.

With this purpose there has been created in the University of Pennsylvania a Department of Neuro-otology, devoted exclusively to this work; and in the past year and a half we have examined

<sup>1</sup> Read before the American Otological Society, June 3, 1916.

125 pathological cases.<sup>2</sup> While giving full heed to the aural aspects, with treatment of any local conditions requiring it, study has been especially directed to the intracranial side of the subject, guided and aided by Drs. Mills, Weisenburg and others on the neurological side and by Dr. C. H. Frazier on the surgical. For this purpose the pointing reactions have far surpassed the nystagmic; and most of our stress will be placed in this paper on these later developments of the Barany testing. Of the intracranial cases eighteen have come to operations and four to autopsy. These sections, antemortem or postmortem, have shown the deductions from the ear-examinations to have been remarkably accurate, and have led us to believe that this work is valuable and worthy of this preliminary report.

As usual in such complex and many-sided researches, anomalous or contradictory findings frequently confront us. Physiological phenomena, not to speak of the psychic, do not group themselves so readily under simple laws as do the merely physical. Yet some inconsistency of findings, even in the same case, marks the vital characteristics of our subject—we are dealing with advancing processes not with fixed morbid lesions; and the variations may be most instructive when understood, however disconcerting they may at first appear to one who vainly undertakes to demonstrate a reaction previously present.

It is hardly necessary at this time to describe in detail the technic of examination. In brief, however, as regards the pointing reactions, the normal person is always aware of the location of his hand or finger in space when his eyes are closed; and he is able with it to find an object previously located by him, as, for example, the finger of the examiner held in front of him. With the ear stimulated, either by cold or hot water or air or by turning in a smoothly revolving chair, he is no longer able to find the finger, but points *past* it in a definite direction, either to one side or the other, above or below, depending upon the exact stimulation employed. These "past-pointing" reactions are absolute in the normal; their modification marks the abnormal and challenges us to find the explanation and locate the fault.

If the right ear is doused with cold water of a temperature of 68° F., the normal person points to the right; if the right ear is doused with hot water of 112° F. he points to the left. This is true, in both instances, also of the wrist, elbow, foot, head, and trunk. Or if the patient is turned in a rotating chair toward the right and then suddenly stopped, all the pointings will be toward the right, and *vice versa* after turning to the left. In each of these tests the head must be rigidly supported in the chosen position.

There has been so much needless confusion, however, in the descriptions of these tests, especially in stating the direction of the nys-

<sup>2</sup> Also many more not found pathological, although we cannot emulate a colleague who claims, "I apply the labyrinth tests to every case coming to the clinic."

tagmus in comparison with the past-pointing, that perhaps we may venture to suggest an absolutely reliable and easy method of remembering these facts. Thus, the usual routine methods are by cold water and turning: now if to the right (that is either turning to the right or douching the right ear) everything is to the right—all the pointings, shoulder from above, shoulder from below, elbow, wrist, neck or trunk, and the falling reactions, all are to the right. Now the deviation of the eyes, just as all the other reactions, is also to the right; but this is the slow movement of the eyes to the right. The "recovery," the quick movement to the left, however, the cerebral component, is more conspicuous, and therefore this phenomenon has been called "nystagmus to the left." *Vice versa*, to emphasize this: if the left ear is douched or the patient is turned to the left, all reactions are to the left and the true vestibular movement of the eyes is also to the left, although mistakenly the nystagmus is spoken of as toward the right. This makes it very simple, especially in teaching students; but to tell them, as does Barany, that the past-pointing is always in a direction opposite to the nystagmus, is not only confusing but misleading; simply tell them—if to the right, everything is to the right; if to the left, everything is to the left.<sup>3</sup> As to the reasons for these reactions:

First as regards the nystagmus, this seems easy and fairly understood. The stimulus travels from the ear to the muscles of the eyes, producing a movement to one side; the quick readjustment in the opposite direction is the cerebral attempt to overcome the abnormal movement. Second, a normal person past-points either to the right or the left, according to the stimulation, because he has a disturbed sensation of his position in space.

Now for a normal person to point, under stimulation, in any direction, there must be a definite arc, just as there must also be a definite tract from the ear to the eye, in order to produce nystagmus. In addition, if douching the ear or rotation produces vertigo, it also naturally follows that there must be an arc from the ear to the subjective centres, which can perhaps be best spoken of as the subjective arc. If, therefore, there should be after stimulation an absence of nystagmus, an absence of past-pointing or an absence of vertigo, we can assume an interruption or lesion along the line of the arc concerned. This is at the basis of this matter of the encephalic localization. The ear is stimulated, the impulse is carried by means of the VIII nerve to a group of nuclei in the lateral part of the medulla, namely the Deiters's nucleus, triangular nucleus, and von Bechterew's nucleus; from here the impulses go in a number of directions. One set goes from the nuclei to the posterior longi-

<sup>3</sup> Is it not time to select a substitute for this misleading word "nystagmus," now hopeless, unless in a general sense, in this connection? In anesthesia or stupor the reaction is solely a conjugate deviation. Why not call it the nystagmic deviation?

tudinal bundle and from here to the VI, IV, and III nuclei in the pons and crus, thus causing a nystagmus; this is definite and in all probability accurate.

As for the cerebellar circuit, it may take many years to work it out positively. Our present conception is that on each side the fibers from the *horizontal* canals go to the Deiters's group, thence to the cerebellum by way of the juxtarestiform body (which is the internal portion of the inferior cerebellar peduncle) through to the cerebellar nuclei, globosus, fastigii, and emboliformis, and then to the cortex of both sides. The fibers of the *vertical* canals apparently have an entirely different course, going directly to the posterior longitudinal bundle, probably entering the cerebellum through its middle peduncle. Another group of fibers undoubtedly goes to the spinal cord.

We have come to a definite conclusion that all pointing reactions are primarily *cerebral* and not cerebellar, as generally stated. When one of ourselves is tested and, for example, with erect head is turned to the right, he has on stopping a subjective sensation of turning to the left. For this reason he feels that he is leaving the finger of the examiner behind him and points to the right, where he conceives the finger now to be. He deliberately points to the right unless by a non-automatic, calculated correction he overcomes the misconception of the position of the finger. If after the usual past-pointing the examiner's finger is moved out to meet that of the examined, who then repeats the test, he past-points almost as much farther to the right, and would continue perhaps to the completion of an entire circle in his chase of the seemingly moving finger but for the limitations enforced by his seating. Yet if rotated and asked to make the same movements of the arm without any finger to touch, he maintains it in the same body-plane with little or no deviation, since he conceives this plane to rotate with his seemingly revolving body. There is, therefore, no cerebellar or automatic drawing of the arm to one side; the past-pointing is purely cerebral. Yet we have it achieved through the synergising action of the cerebellum: with the cerebral mandate is associated the cerebellar influence, the muscle-sense, arthrodial sense, tactile, auditory, and visual impressions and memory. In fact, the pointing reactions are dependent on so many things that it is necessary to assume a complicated arc to be able to explain them.

The movement, therefore, is initiated by the cerebrum, and whatever deviation occurs is because the ear-stimulus has given by artificial means a false conception of the position in space. If we postulate that the sense of direction of the right arm is determined by a stimulus going from the ear to that particular centre of the cerebellar cortex governing the right arm, and from there through the superior peduncle of the cerebellum to the cerebral cortex, and similarly an entirely separate tract of fibers for the left

arm centre, we then can explain why any disturbance along the line of the right arm tract will cause a lack of past-pointing of that arm alone, whereas all other parts would past-point because their circuits are intact.

In conclusion, we can claim that by these valuable ear-tests we can usually differentiate lesions of the labyrinth from those of the cerebellum; we can always tell when the VIII nerve is diseased; we can say positively also whether or not the posterior longitudinal bundle is affected; and we can detect a lesion of the cerebellum but cannot always locate it.

We offer here two contributions that so far as we know are new:

1. The subjective circuit. We postulate this circuit *through the cerebellum* to the higher centres and in proof cite: (a) two patients who had perfect nystagmic reaction but no past-pointing and no vertigo; (b) several cases of spontaneous nystagmus with no vertigo; (c) in most cases of cerebellar lesion dizziness is either absent or subnormal; (d) a patient with no nystagmic reaction and yet normal past-pointing and vertigo. As the two latter reactions seem to go together, it may be concluded, at least for the time being, that the impulses which are concerned with the vertigo pass through the cerebellum. Also, arguing backward, if no vertigo is obtained it may prove that there is a lesion of the cerebellum.

2. Our second postulate is that the fibers from the different semicircular canals have entirely *separate tracts* of their own; the horizontal canal has an entirely different set from the tracts for the superior canal. This we have proved in 28 cases by means of the following phenomena: In all of these there was little reason to doubt that the region of the posterior longitudinal bundle was implicated. In each of these cases douching of the superior canal (that is with the head upright) produced neither nystagmus, past-pointing, nor vertigo; whereas on stimulation of the horizontal canal (with the head back 90°) all the reactions came through promptly—nystagmus, past-pointing, and vertigo. It is therefore evident that there is a complete central differentiation for the different canals of all three tracts, remembering that in none of these cases was there a peripheral lesion. Autopsy or other findings in some of these cases with no involvement of the horizontal canal fibers of either side, yet with no passing of the stimulus by the superior canal fibers, showed that in the medulla and pons the fibers for the superior canals are mesially located, whereas the horizontal canal tracts are external.

Further details might be given as showing the possibilities of scientific research in these lines, namely, the finding and defining of encephalic tracts by means of these ear-tests. Furthermore, it is not improbable that we shall be able to locate in the trunk of the VIII nerve more definitely than we have yet done the relative

positions of these bundles of fibers, as has been partly done with much value in the optic nerve. Just as the older anatomists recognized that the "portio molis" and "portio dura" could be wholly differentiated into the acoustic and the facial nerves of different origin and function, and as later research is separating the cochlear from the vestibular and intermediary nerves, so it is our part more minutely to differentiate these trunks into their components and by tracing their encephalic course to improve our diagnostic possibilities, with further practical refinements in localization. To this good task we invite the aid of all our colleagues.

### FURTHER EXPERIMENTATION IN ANIMALS WITH A MONILIA COMMONLY FOUND IN SPRUE.<sup>1</sup>

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IN a paper read before the Association of American Physicians May 13, 1915, entitled "Studies in Moniliasis of the Digestive Tract in Porto Rico,"<sup>2</sup> and in one read before the Medical Society of the District of the North of Porto Rico, March 18, 1915,<sup>3</sup> reference is made to incomplete results of animal experimentation with a new monilia found in sprue, promising additional observations. This paper is in continuance of these experiments, and although experimental moniliasis in animals is yet in its infancy, nevertheless, some striking results in a short series seem to warrant prompt mention, the writer realizing, however, that these rapid preliminary investigations should only be understood as mapping out future and more elaborate lines of study.

As will be seen by reference to the above-cited papers and others of recent date, "Is Sprue a Moniliasis of the Digestive Tract,"<sup>4</sup> and "The Dietetic Treatment of Sprue,"<sup>5</sup> there is justification for considering Balr's opinion that sprue is due to a monilia as correct, as well as for admitting, as will be seen, that this organism is not *Monilia albicans*, at least in Porto Rico, but as far as can be determined a distinct and heretofore undescribed species, which I have

<sup>1</sup> Read by title before the Academy of Medicine of Porto Rico.

<sup>2</sup> AM. JOUR. MED. SCI., 1915, cl, 680.

<sup>3</sup> JOUR. AM. MED. ASSN., 1915, lxiv, 1893.

<sup>4</sup> AM. JOUR. TROP. DIS. AND PREV. MED., 1915, iii, 32.

<sup>5</sup> Now being published by AM. JOUR. TROP. DIS. AND PREV. MED.



found in now nearly 100 cases of true sprue and in but a small percentage of carriers.

All work upon animals up to date will be succinctly stated, and finally tentative deductions will be drawn therefrom.

**HYPODERMIC INOCULATIONS.** *Rabbit I.* Received on December 26, 1914, five drops of a seven-day glucose bouillon culture, 2 per cent. plus 1, in the muscles of the tongue. This was a pure culture from Case IV, isolated in November, 1914, from the inflamed tongue of a typical case of severe sprue whose history was chronicled in "Clinical Notes on a Case of Sprue."<sup>6</sup> This case, thought to be recovering, relapsed and died in the United States early in 1915. The diagnosis was not only confirmed by consulting physicians here in Porto Rico, but was independently made in New York by Crow, of the U. S. Navy, and tacitly accepted as sprue by the *Tropical Diseases Bulletin of London*, March 15, 1915, No. 4, iv, 225. This strain, therefore, has been used in all save one or two instances in animal experimentation, and culturally and morphologically is identical with all others isolated as *Monilia X* from my cases of sprue.

In the operation of hypodermic injection of the dose into the tongue the animal received also about 2 c.c. per oram. After forty hours diarrhea began and the animal was seized with great trembling, falling about as though intoxicated. At times it would scream out and then lapse into a semicomatose condition, its snout gradually falling to the floor of the cage, upon which contact it would endeavor to straighten up and brace itself in a sitting posture. Much abdominal gas was developed and the mucous membranes were purplish. Death in seventy-five hours.

*Autopsy.* Tongue presents a dark congested spot at the site of injection, which revealed in section a necrotic area, surrounded by a wide zone of inflammation.

Stomach shows a white grumous coating filled with yeasts. Small intestine likewise so coated, and entire intestine full of gas. Right heart filled with blood. Lungs highly congested, as were liver and spleen. Kidneys large and congested, and all save heart were friable, punctuated, on section, by minute white dots.

Pure culture of *Monilia X* directly obtained from the following organs: spleen, liver, kidneys, lungs and heart's blood, no contaminating organism being found. Also from the necrotic spot in the tongue, and the mucous membrane of the stomach and small intestine. Cultures from the surface of the tongue were negative for yeasts.

Microscopically the liver and kidneys were examined, the former showing an occasional yeast; the latter demonstrated large emboli-like colonies in the cortex, with surrounding zone of intense inflam-

<sup>6</sup> Bol. Assoc. Med. de Puerto Rico, 1914, x, 10.

mation. It is interesting to note the prevalence of short hyphae and oval forms in the kidney. Stain: Gram-Weigert fibrin method and Bodin's victoria blue and erythrosine. As these emboli-like colonies in the kidneys were thus identified as "the minute white spots" mentioned in the gross anatomy of organs of animals dying after infection by monilia it is presumable that all these necrotic areas were similar.

After five months, during which the original culture had become old and full of mycelium, and had also been several times replanted, Rabbit II (A and B) received 5 c.c. each of a thirty-day culture in sugar-free bouillon of Monilia X from same case (IV) by intraperitoneal injection. No effect whatsoever after two weeks, save possible temporary intoxication upon injecting the dose. This appeared in a half hour, and had disappeared in about three hours. Rabbit II (B) received four or five consecutive inoculations of the same culture in 10 c.c. doses without effect, save the temporary intoxication above noted. Despairing of a successful inoculation of these two animals intraperitoneally, I injected 5 c.c. of a week-old culture in glucose bouillon into the connective tissue of the ear of Rabbit II A. My original intention was to give an intravenous injection, but the squirming and kicking of the animal caused me to discharge the dose instead into the connective tissue. There was no effect whatsoever upon the rabbit's apparent general health, but within three weeks the ear became the site of a huge "blastomycotic ulcer," which slowly healed of itself.

*White Rat I.* Repeatedly injected intraperitoneally with 1 c.c. of the thirty-day culture of Case IV as in the case of Rabbit II (A and B). No effect after three weeks' observation. He then received 4 c.c. of a five-day culture in glucose bouillon, 2 per cent. plus 1 from Case XV, a severe and typical case of sprue, originally recovered from the patient but five weeks before, and after having been passed through Rat III. Death in eighteen hours.

*Autopsy.* Lungs highly congested. Liver, spleen, and kidneys dark red and friable. No peritonitis. Cultures from all organs positive for Monilia X.

*White Rat III.* Received intraperitoneally 5 c.c. of a ten-day culture in saccharose bouillon of Monilia X from Case XV. Died in the night, five days later. An interesting feature of this case was that the site of injection necrosed, exposing the intestines over a space 1.5 cm. in diameter.

*Autopsy next morning.* Rigor mortis marked. Ulceration of abdominal wall over an area 1.5 cm. in diameter, leaving a perforation communicating with the interior of the peritoneal cavity. Lung deeply congested; spleen small; liver congested. Cultures from spleen and liver positive for Monilia X.

*Guinea-pig II.* Received intraperitoneally 1 c.c. of a glucose bouillon culture, 2 per cent. plus 1, of Monilia X recovered from

Case XCII (*a*), a severe advanced case of sprue. Daily injections were given beginning August 19. Cultures for first three injections were one week old. Thereafter from August 25 fresh cultures were substituted: the first twenty-four hours old; the next forty-eight hours; and so on until, on August 31, the animal died, having received that day 1 c.c. of a 168-hour culture. Death in twelve days.

*Autopsy.* Performed immediately. Lungs highly congested with minute white spots. From all organs typical colonies of *Monilia X*.

*Guinea-pig III.* Received intraperitoneally 1 c.c. of a forty-eight-hour glucose bouillon culture, 2 per cent. plus 1, recovered from Guinea-pig II. Death in forty hours.

*Autopsy.* Performed immediately. Only gross changes found were high congestion of lungs, spleen, and liver, which were friable and filled with minute white nodules. Cultures from lung, liver, and heart's blood typical of *Monilia X*. Cultures of a monilia recovered from the excreta were atypical.

*Guinea-pig IV.* This animal received 1 and 2 c.c. doses, intraperitoneally, of the old non-virulent cultures from Case IV, used unsuccessfully on Rabbit II, A and B, and White Rat I, as above detailed. By this time the culture, however, had been growing for nearly a year in Sabouraud's glucose agar, 4 per cent. plus 2, with monthly transplantations. The cultures injected were a week old in glucose bouillon, and were given daily for nine days. On the tenth day 5 c.c. were injected and the animal died the next morning.

*Autopsy.* Immediate. Usual macroscopic findings. The original monilia was recovered from the peritoneum, diaphragm, spleen, adrenals, and mucous membrane of the bladder.

*Guinea-pig V.* Received intraperitoneally 1 c.c. of a forty-eight-hour culture of the organism recovered from Guinea-pig IV. Death in ten hours.

*Autopsy.* Lungs, liver, spleen, and kidneys highly congested with white spots. Peritoneum normal. Typical colonies of *Monilia X* recovered from kidney, spleen, heart's blood, and lung. Peritoneal fluid negative for monilia. The organism recovered from this animal killed animals after ingestion of its cultures, as will be seen later.

*Guinea-pig IX.* Received 1 c.c., intraperitoneally of a six-day glucose bouillon culture, 4 per cent. plus 1, obtained by culture from kidney of Guinea-pig V. Time to kill not known, but was within twenty-four hours.

*Autopsy.* Died during night and autopsied next morning. The only thing of note was a high degree of congestion of lungs with its corresponding minute white spots. No peritonitis. Cultures from liver, spleen, and kidney gave colonies typical of *Monilia X*. Heart's blood and lung negative.

*Guinea-pig X.* Received intraperitoneally 1 c.c. of a six-day glucose bouillon culture, 4 per cent. plus 1, of *Monilia X* recovered

from Guinea-pig III (Case XCII (a)). Died within twenty-four hours in convulsions.

*Autopsy.* Hemorrhagic fluid in peritoneum. Lung highly congested with minute white spots. Cultures from kidney, heart's blood, liver, spleen, and lung positive for Monilia X.

*Guinea-pig XII (b).* Received intraperitoneally 1 c.c. of a glucose bouillon culture, 4 per cent. plus 1, of Monilia X recovered from Guinea-pig VIII, which had died after ten days' feeding on culture of the monilia recovered from Guinea-pig V. This experiment was primarily made to sustain the virulence of the strain recovered from autopsy of Guinea-pig VIII. Died in seven hours.

*Autopsy.* Immediate. Considerable increase in peritoneal fluid. Bladder full of urine, which has a heavy sediment. Lung highly congested with white points. All abdominal organs friable and dark red. Cultures from spleen, liver, urine, kidney, peritoneum, stomach, and lung were made, but only liver, lung, and peritoneal fluid were positive for Monilia X.

*Guinea-pig XII (a).* Same as above, but died in twenty hours. Culture from spleen positive for Monilia X.

*Guinea-pig XVII.* By intraperitoneal injection of 1 c.c. of a five-day glucose bouillon culture, 4 per cent. plus 1, of Monilia X recovered from the spleen of Guinea-pig XII (a). Death in nineteen hours.

*Autopsy.* Increase in peritoneal fluid; bladder full of urine; much gas in intestines; friable, dark red abdominal organs; minute white spots in liver, spleen, and lungs. Testicles highly inflamed. Cultures from peritoneal fluid, liver, spleen and testicles positive for Monilia X.

FEEDING EXPERIMENTS. *Guinea-pig I.* On the strength of advice given by French authors that animals may only be made susceptible to infection by certain yeasts in a condition of reduced vitality from underfeeding, this animal was fed for a week on a patent malted baby food alone, a food to which it was foreign, and one offering excellent pabulum for monilia. Beginning January 8, 1915, 10 c.c. of a fresh bouillon culture of Monilia X from Case IV was daily mixed with this food. Within three days he became very ill and seemed about to die. Had diarrhea and was somnolent. Death on January 25, 1915, seventeen days after the feeding with cultures was begun.

*Autopsy.* Performed eight hours after death. Animal somewhat emaciated. Tip of tongue pink but no mouth lesions. General glandular enlargement, chiefly of submaxillary glands, but the axillary and inguinal glands were also increased in size. Section of all glands showed a high degree of inflammation. Liver and spleen were highly congested and friable. Lungs and kidneys were the same, but to a less extent. Stomach and small intestine were covered with a creamy, grumous coat; stomach congested in spots; intestines highly congested. Bladder filled with urine.

Peritoneum normal. Cultures from lung, cervical and inguinal glands, small intestine, heart's blood, kidney, and liver were all negative. Cultures from spleen, tongue, and stomach gave colonies of monilia. All save culture from the spleen were identical with Monilia X.

*Guinea-pig VIII.* In the case of this animal it was determined to depend entirely upon a hypervirulent monilia, previously passed, as has been seen, through Guinea-pigs IV and V, and to allow the pig to eat its malojillo grass undisturbed by the addition of any carbohydrate. These cultures were merely poured over the grass. 10 c.c. per diem of a seven-day glucose bouillon culture of the monilia recovered from Guinea-pig V was thus administered. On each subsequent day the culture was one day older, as all were sown the same day. The absence of Monilia X from the feces was previously determined. Feeding began September 17, 1915. On September 29 the animal was very sick, with hair on end, abdomen distended with gas, and lips and nose fiery red and raw. The animal died during the night.

*Autopsy.* September 30, 10 A.M. Animal slightly emaciated. All around the borders of the mouth, especially at the angles and inside the lips, the mucous membrane was red and raw. The entire lower portion of the nose was raw and blood issued from both nostrils. Raw area on the inside of the right cheek. From the upper border of the lip to half an inch above the level of the nostrils and for one-eighth inch external to same, denuded. Tongue apparently normal. The subcutaneous tissues of the animal were congested from the level of the ensiform appendix upward, this being especially noticeable in the neck. The submaxillary and cervical glands were highly inflamed, congested, and swollen, and of a dark red color. Lung highly congested, especially posteriorly, and was filled with minute white spots. The liver and spleen were dark red and friable, the liver being enlarged. The kidneys were twice their natural size and dark red. Peritoneum apparently normal, but there was an excess of blood-tinged peritoneal fluid, without adhesions or pus. Bladder filled with urine. Stomach and intestines a lively pink. Lower bowel normal.

Cultures from the excoriated mouth and nose, small intestine, stomach, tongue, esophagus, and lung were positive for Monilia X. Submaxillary gland, lumen of the trachea, cervical glands, kidney, heart's blood, peritoneal fluid, liver, and urine in bladder were negative.

*Guinea-pig XI.* Six healthy guinea-pigs were chosen, and one other which had been partially immunized by six small doses, injected intraperitoneally of a virulent culture of Monilia X. They were all placed under the same conditions in the same division of a cage. In the adjoining division, separated by a wooden partition for half the height of the cage and wire netting for the upper half, were other healthy control pigs. The seven experimental animals

received upon their ration of malojillo grass 48 c.c. of a six-day glucose bouillon culture of *Monilia X* recovered from Guinea-pig VIII. This was poured over their conjoint food, a dose of 7 c.c. to each a day. These feeding experiments began October 6, 1915. On October 7 the smallest pig (XII A) died.

*Autopsy.* Immediate. One roseolous spot on the upper lip. The submaxillary glands were swollen and inflamed. No peritonitis, but increase in peritoneal fluid. Bladder full of urine. Large intestine full of a fermented liquid and distended with gas. Lung highly congested, and this organ and the spleen showed minute white spots. Kidneys and liver congested and enlarged.

Cultures from kidney, lip at site of inflammatory spot, tongue, heart's blood, stomach, spleen, and large intestine positive for *Monilia X*. Contents of gall-bladder and peritoneum were negative.

The rapid death of this animal after a day's feeding naturally aroused my suspicion that it had fallen a victim to an epizootic at times observed among guinea-pigs here and chronicled in standard works, but the prompt demonstration of *Monilia X* in the above-mentioned organs caused me to attribute its death to the organism upon which it had fed.

*Guinea-pig XI B.* Died October 8, forty-eight hours after beginning experiment.

*Autopsy.* Increase in peritoneal fluid, which is of a citrine color. Bladder full of urine. Intestine very full of gas. Lung congested with minute white spots. Solid organs of abdominal cavity dark red and friable. Cultures from tongue and lung positive.

*Guinea-pig XI C.* Died October 12, six days after beginning the experiment.

*Autopsy.* Increase in peritoneal fluid. Bladder full of urine. Intestine full of gas. Lung congested with minute white spots. Solid organs in abdominal cavity dark red and friable. Cultures from tongue, lung, stomach and liver positive.

*Guinea-pig XI D.* Died October 13, seven days after beginning experiment. Autopsy same as for Guinea-pig XI C. Cultures from tongue and liver positive for *Monilia X*.

*Guinea-pig XI E.* Died October 13, seven days after beginning experiment. Autopsy same as C. Cultures positive from several organs for *Monilia X*, but record was lost.

*Guinea-pig XI F.* Still living.

*Guinea-pig XI G.* This pig had received intraperitoneally, beginning September 17, 1 c.c. of a glucose-bouillon culture from the spleen of Guinea-pig V. The culture was thirty-six hours old when first injected, and 1 c.c. was given daily for six days; the culture being, of course, one day older at each injection, as the six tubes were sown the same day. The animal sickened but did not die. Feeding began, as has been seen, on October 6, and the animal died October 20.

*Autopsy.* Nothing of note. Cultures were negative from all organs save the stomach and intestines, which were positive for Monilia X.

*Monkey II.* A small brown monkey was subjected to a preliminary diet similar to Guinea-pig I for a week, then to this food was added 10 c.c. daily of fresh glucose-bouillon cultures of Monilia X from Case IV. The animal promptly began to suffer from diarrhea a few days thereafter, and continued to have very frequent pultaceous, gray movements with much gas during the six weeks the feeding was kept up, and for some weeks after the rigid diet was suspended, and he was given his normal food without the admixture of Monilia X. During all this time he steadily lost in weight, became quite inactive, and seemed quite sick. He eventually recovered.

*Monkey III.* Large black monkey, weighing four pounds before beginning experiment, who had lived in a cage near my laboratory table for a year, having thus been under my constant daily inspection. This animal had never had diarrhea, and had always seemed healthy. His stools had been sown for monilia, and always yielded a completely different species, culturally and morphologically, from Monilia X. On October 4, 10 c.c. of a six-day glucose bouillon culture from Guinea-pig VIII was twice daily mixed with his normal food. Forty-eight hours afterward he began to have diarrhea, which rapidly became severe, and has so continued to date (six weeks), with intervals of a day or two of respite. In these six weeks the animal has lost one and a half pounds in weight, but he is usually active only occasionally seeming to be sick. He has had no mouth lesions nor excess of gas. His feces are loaded with Monilia X.

OBSERVATIONS. 1. The species of monilia recovered by me from now nearly one hundred cases of sprue, and apparently a new species from careful cultural and morphological investigations, is a pathogen for current laboratory animals by hypodermic inoculation.

2. This species, which I will for the present call Monilia X, is ordinarily a low virulence organism.

3. When recovered from a patient with sprue and promptly injected into certain laboratory animals it generally produces their rapid death from a mycotic septicemia.

4. When grown for a long time and frequently transplanted the same organism which rapidly killed soon after isolation from a sprue patient seems to partially or completely lose its virulence.

5. This virulence may be recovered by passage through susceptible animals, and even reach such a point as to sicken or kill these animals by continued feeding.

6. Ordinarily an animal may not be killed by feeding Monilia X when first isolated from a sprue patient. Its virulence must be augmented by passage before uniform pathogenicity through feeding can be demonstrated.

7. In such animals the symptoms depend on the part of the intestinal tube must affected, in the portion in which these monilia secure their first foothold.

8. A certain number of animals exposed by feeding, rapidly die of a monilia septicemia believed by me to be due to a sudden primary pneumonia and secondary septicemia.

9. Animals escaping this fate succumb more slowly to what seems to be a toxin developed in the intestinal tract by a localization of these monilia.

10. Feeding experiments have resulted in the production of a stomatitis on two occasions and in the appearance of severe and long-continued diarrhea in several occasions.

11. Monilia septicemia causes the necrotic areas in animal organs referred to as "white spots" macroscopically. This has been verified microscopically in kidneys, and presumed to be the same for all organs so affected. Such organs are highly congested, dark red, and friable.

12. Localized in the skin, typical blastomycotic ulcers are formed whose characteristic is necrosis without pus formation. If an internal organ is attacked large colonies of monilia are seen which look like emboli. Intervening spaces are generally free from the organism. This explains a casual failure to obtain a successful culture from an evidently infected organ, and thus differs radically from a bacterial septicemia.

13. Microscopically, infected organs show large clumps of monilia surrounded by an intense inflammatory zone. I have never seen pus produced by monilia.

14. In one guinea-pig presenting a severe stomatitis, sections of the affected zone revealed monilia in the midst of the muscular bundles below the subepithelial connective tissue. This may explain the tendency for sprue to recur after an apparent dietetic cure: the yeasts are starved out in the surface; the patient apparently recovers, and, later, the deep lying roots of the mycelia layer push out toward the surface and reestablish a surface growth with its consequences and a relapse.

15. In experimental animals in whom mycotic septicemia is induced by intraperitoneal injection the lungs are the most grossly affected; after them the kidneys and microscopic examination corroborate the gross anatomy.

A forthcoming monograph is contemplated with detailed description of morphological and cultural studies of this organism, and illustrations drawn by the artists of the Institute.

My acknowledgements are made to Drs. W. W. King and González Martínez for valuable assistance in autopsies, and to Messrs. José Loubriel and Damián Artau, Technical Assistants of the Institute, for assiduous care of animals and assistance in autopsies.



## THE PRESENT STATUS OF THE ELECTROCARDIOGRAPHIC METHOD IN CLINICAL MEDICINE.\*

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A GALVANOMETER suitable for taking clinical electrocardiograms was designed by Einthoven in 1903. Nine years ago (1906) the method was perfected and became available for general use. The first papers dealing with the results of clinical electrocardiography appeared six and seven years ago (1908 and 1909). The first American papers were published in 1910. This report, then, records the results of observations extending over a period of less than ten years.

The electrocardiogram is a record of the electrical discharges from the heart during its activity. Its chief merit consists in the fact that its form remains constant from a time shortly after birth until the alterations due to old age set in. If it changes at all, it does so as the result of alterations within the heart, or in the position of the heart within the body. An alteration from the accustomed form therefore represents a change which must be looked upon as significant.

A normal electrocardiogram in reality does not exist. A group of normal persons in the prime of life yields electrocardiograms which vary only within certain limits. They tend, naturally, to resemble one another, and from this circumstance an ideal form, regarded as the normal electrocardiogram, has been evolved. The constant form of electrocardiograms depends in part on the fact that the method of obtaining records is free from errors due to personal equation. If electrocardiograms are taken with a standard instrument, in a standard way, they may be made anywhere by anybody, and should yield identical curves.

The constancy of an individual electrocardiogram, then, is the basis of the method's importance. Compared with any other form of graphic record of circulatory phenomena, this advantage is manifest. No other one is so simple to read. It can be taken without difficulty at any period of life, and without any discomfort to a patient. It cannot, of course, displace other graphic methods when these record activities other than those given in the electrocardiogram. But where information is required which can be obtained by two methods, the electrocardiographic and another, the electrocardiographic is simpler and more reliable.

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The well-established form of the so-called normal electrocardiogram is the basis of the value of the abnormal one. The normal one depends on the orderly performance of a number of functions. An abnormal one results when the orderly performance of one or more of these functions is no longer possible. Four main cardiac functions on which the normal curve depends can now be recognized. In the first place, it depends on the orderly *passage* of impulses, or more correctly on the orderly spread of electrically excited states through each pair of cardiac cavities, and on the duration of such states in each part of the chambers. It should be noticed that the *production* of impulses cannot be detected in the electrocardiogram, but only the electrical states which the activity of the impulses has initiated. In the second place, the normal electrocardiogram depends on the orderly *sequence* of contraction\* of the auricles and ventricles. In the third place, it depends on the orderly *coördination* of the muscular mass in each pair of cavities, and finally on the usual *disposition and volume* of the muscular mass of each pair of cavities. The normal electrocardiogram probably depends on other factors besides these, but these are the ones which we can recognize in the records. The orderly performance of these functions is recognized by the accustomed form and by the time relation of the waves. The interpretation of functional alterations in the heart is based, therefore, on the alterations which are seen in the electrical elements (*P*, *R* and *T* waves) which represent them.

I take up in turn the factors which determine the normal electrocardiogram and will enumerate what disturbances in cardiac function the curves permit us to detect. The first function mentioned was the normal *passage of the impulse* in each pair of cavities. When the passage is normal through the *auricles*, it is represented (Fig. 1) by a wave (*P*) having a definite rounded form, a certain duration, and an upward direction.<sup>1 2</sup> The rate of the heart is shown by the frequency of its regular recurrence. The passage of an impulse having an abnormal origin is detected by an alteration in the form of the wave.<sup>3</sup> The most extreme change is an inversion (Figs. 2 and 3).<sup>4</sup> It is supposed to denote that the impulse has arisen at a lower level of the auricles than usual. If the wave is premature, is out of place, it is called an extrasystole (Figs. 2, 3, 4, and 5). Premature auricular beats are usually followed by ventricular contractions. These often have (Fig. 4), but need not have (Fig. 5), the same form as the other complexes in the same individual. Many intermediate forms between the inverted and the normal wave occur. It is not yet possible to correlate each form with a special method of spread of the impulse. But changes in outline may occur (Fig. 6) without substantial

\* We speak of the activity of the cardiac muscle in the usual terms, such as contraction, but it is understood that the accompanying electrical state is the matter of immediate concern.

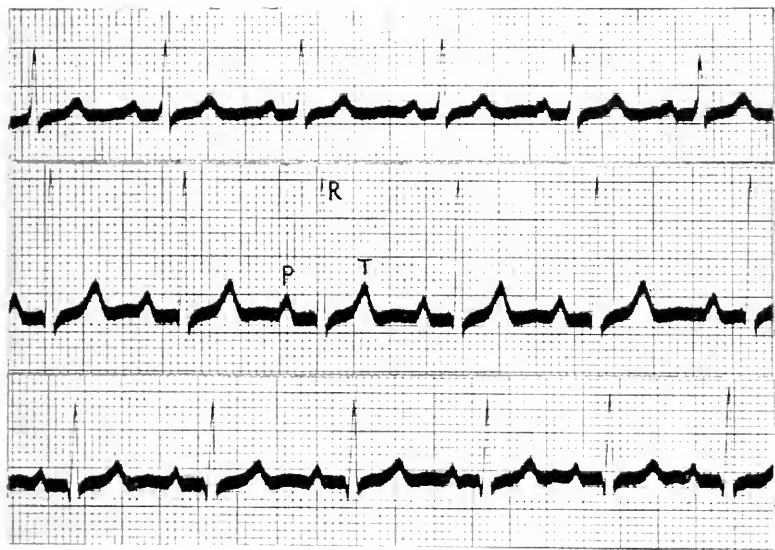


FIG. 1.—Normal electrocardiogram. Leads 1, 2, and 3.

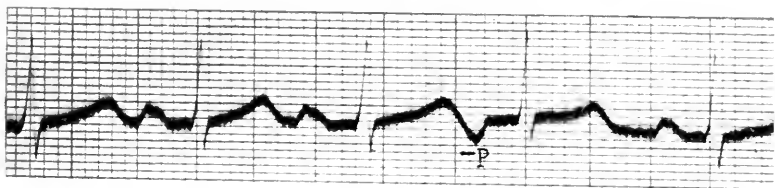


FIG. 2.—In the premature auricular beat (extrasystole) the auricular representative is inverted. Lead 2.

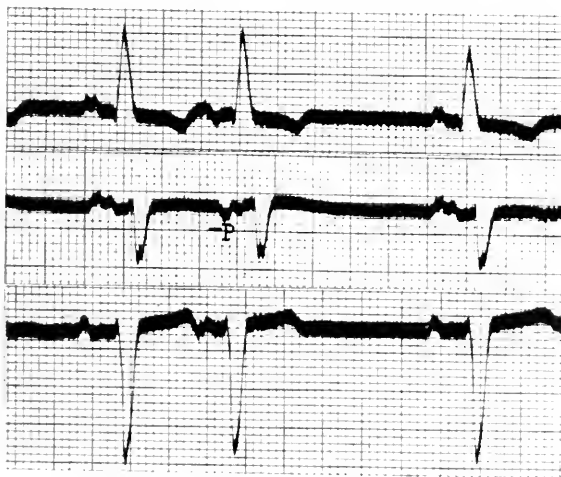


FIG. 3.—A single premature auricular beat taken from each of the three leads is shown. There is a tall *R* wave in *L*<sub>1</sub>; the *R* wave is short and the *S* wave deep in *L*<sub>2</sub> and *L*<sub>3</sub>. In *L*<sub>2</sub> the auricular representative is inverted. The ventricular complexes in the extrasystolic cycles are substantially like the usual beats.

alteration of rhythm.<sup>5</sup> When a given type of abnormal wave recurs in rapid succession, each followed by a ventricular beat, a paroxysm

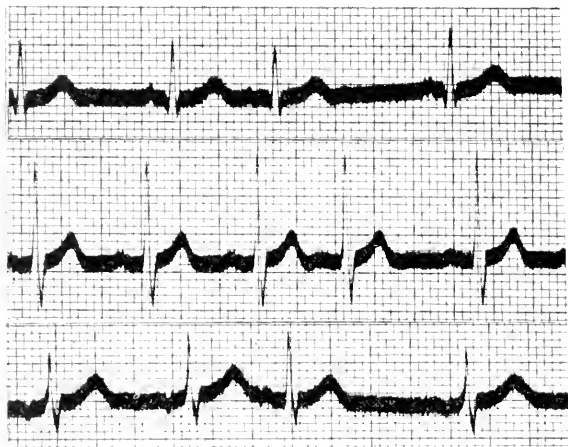


FIG. 4.—A single premature auricular beat taken from each of the three leads is shown. The extra-auricular representatives are like the usual beats. The ventricular complexes are also substantially like the usual beats.

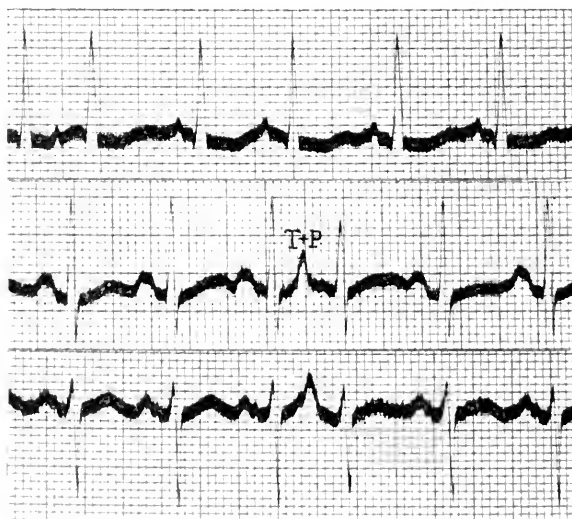


FIG. 5. A single premature auricular beat taken from each of the three leads is shown. The extra-auricular representatives deform the preceding *T* waves. In *I*- and *II*, the *R* and *S* waves following the extra-auricular beats depart from the usual form.

of tachycardia (Fig. 7) exists.<sup>6-7</sup> The clinical diagnosis depends in addition, of course, on the nature of the onset and offset. These

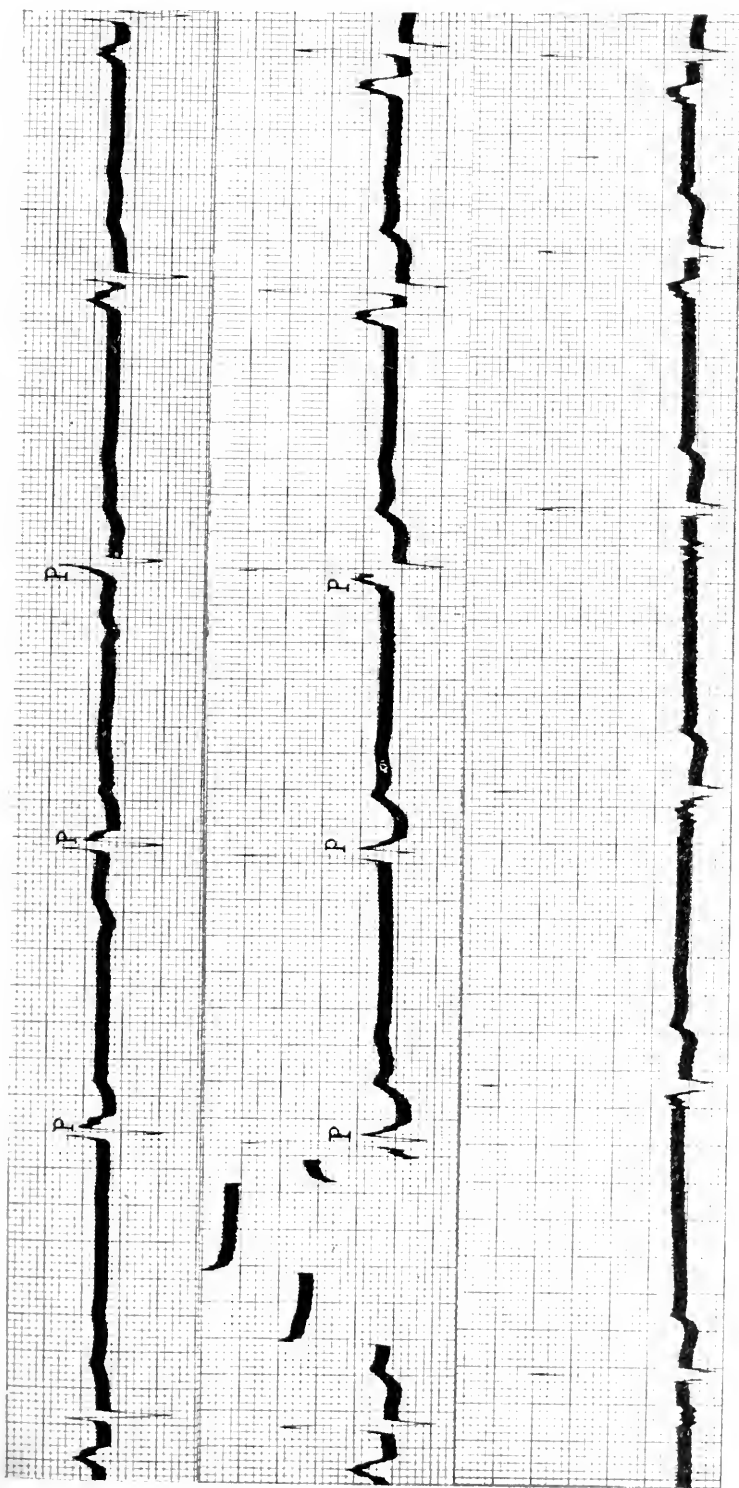


FIG. 6.—A form of nodal rhythm is shown. Leads 1, 2, and 3. Leads 1 and 2 deserve especial attention. They duplicate each other exactly in reproducing an entire phase of the irregularity. The relation of  $P$  to  $R$  waves vary in the same manner in each. In  $La$  the  $P$ - $R$  relation also varies; the sign of the  $P$  waves changes gradually from negative at the beginning to positive at the end of the curve. The  $P$ - $R$  time at the beginning is a trifle longer than at the end of the curve. The patient from whom these curves were taken was under the influence of digitalis.

are the principal auricular changes. In the *ventricles* the passage of a normal wave of excitation is represented by two waves, *R* and

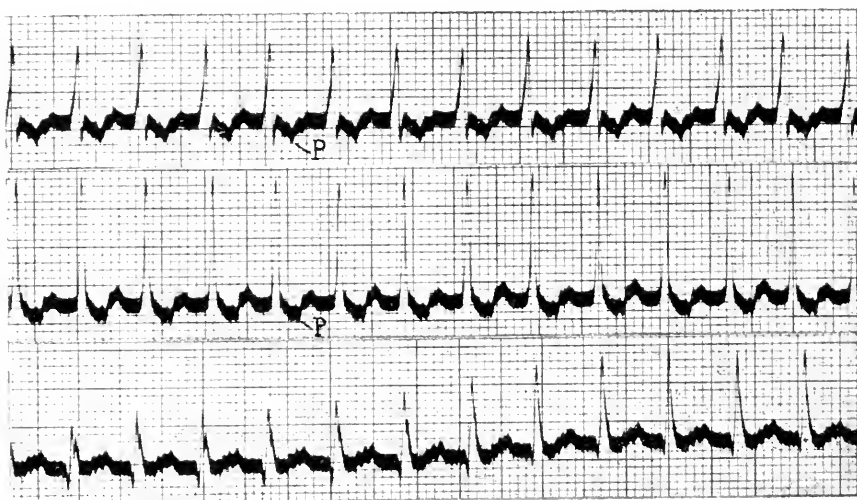


FIG. 7.—A portion is shown of a paroxysm of tachycardia of auricular origin. Leads 1, 2, and 3. The *P* waves in  $L_1$  and  $L_2$  are inverted.

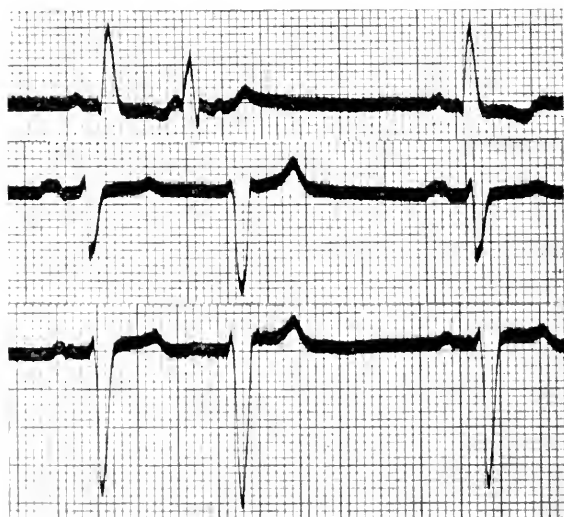


FIG. 8.—A single premature ventricular contraction is shown in each of the three leads. The extrasystole takes its origin in the wall of the left ventricle; there is a tall *R* wave in  $L_1$  and a deep *S* wave in  $L_2$  and  $L_3$ .

*T* (Fig. 1), the first a tall spike, the second a shorter but wider rounded wave, the two separated by a space. Systoles having an



FIG. 9.—A single premature ventricular beat is shown in each of the three leads. In  $L_1$  there is a deep  $S$  wave; in  $L_2$  and  $L_3$  the  $R$  wave is tall. In  $L_1$  an added cycle resembling but differing somewhat from the other complexes follows the extrasystole. An explanation of its significance is not entered upon.

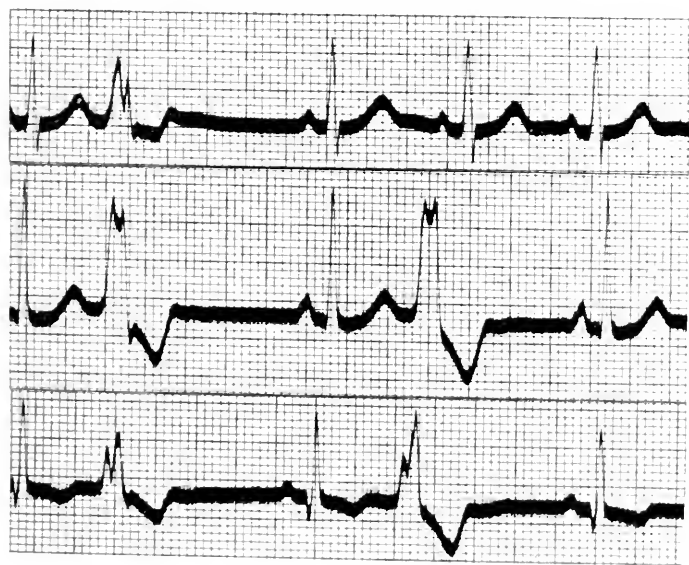


FIG. 10.—Premature contractions in each of the three leads are shown. Here the  $R$  waves are tall in all the extrasystoles.

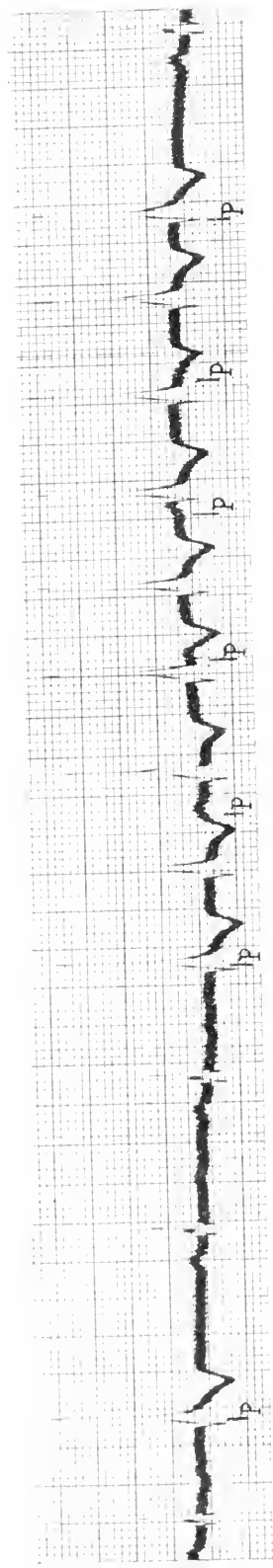


FIG. 11.—A paroxysm of ventricular tachycardia is shown. Lead 3. The paroxysm is composed of a succession of ectopic cycles like the second one reproduced. The paroxysm does not interfere with nor alter the regular recurrence of the auricular beats. Their incidence is indicated in the curve.

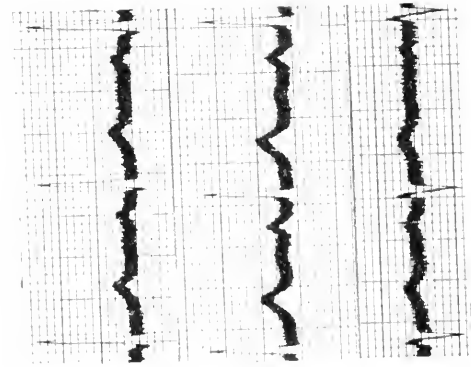


FIG. 12 A

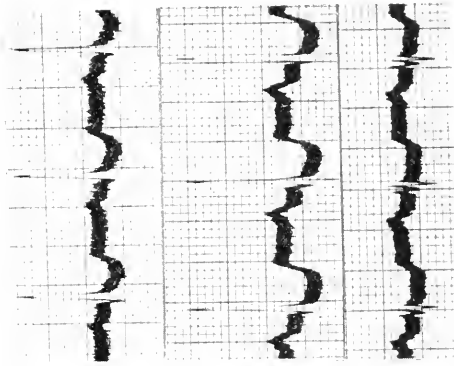


FIG. 12 B

FIG. 12.—A, leads 1, 2, and 3 taken from a patient not under the influence of digitalis. The *T* waves are upright. B, leads 1, 2, and 3 taken from the same patient under the influence of digitalis. The *T* waves are inverted in the three leads.



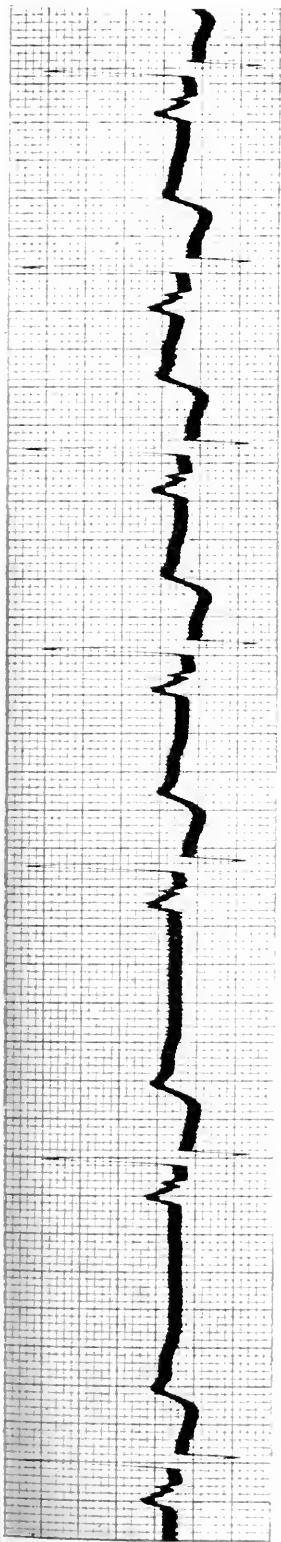


FIG. 13.—Sinus irregularity. Lead 2. The unequal spaces between succeeding cycles is shown.

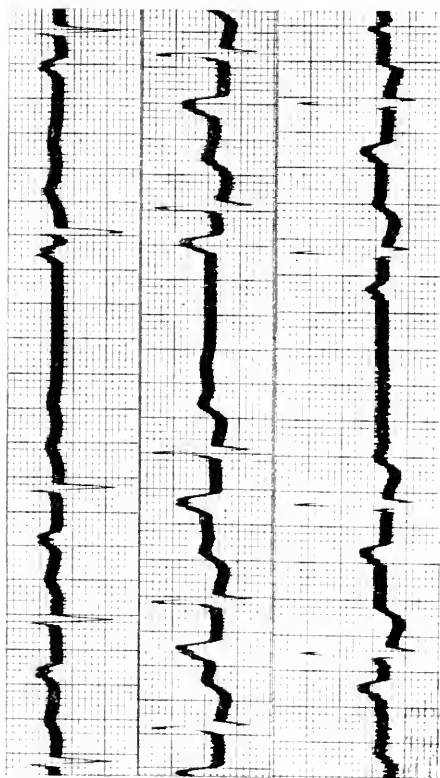


FIG. 14.—Sino-auricular block. Leads 1, 2, and 3. The long intervals between the *P* waves are equal almost to two of the other periods. A moderate sinus irregularity is also present.

abnormal origin are detected by an alteration in the form of either of these waves, the altered form depending (1) on the site where the impulse starts, and (2) on the way the excitation wave travels. If it arises in the wall of the left ventricle it has one form (Fig. 8); if in the right ventricle, it has another (Figs. 9 and 10). When a beat of this nature is premature it is called an extrasystole. A rapid succession of such abnormal beats results in a paroxysm of tachycardia (Fig. 11).<sup>9</sup> Long paroxysms of ventricular origin are rare; usually they consist of a series of not more than twelve to thirty-six beats. In the paroxysm reproduced, two things are clear: (1) that the paroxysm consists of a succession of complexes, precisely like the single extrasystole which precedes it, and (2) the paroxysm leaves the rate and rhythm of the auricles undisturbed. Another alteration concerns the second ventricular wave, the *T*



FIG. 15.—Incomplete auriculoventricular block. Leads 1, 2, and 3. The third auricular representative is blocked in each of the three strips. The patient is under the influence of digitalis. The *T* waves are inverted.

wave, and consists in an inversion (Figs. 12, *A* and *B*). It occurs under the influence of drugs of the digitalis group<sup>10</sup> and probably other agents.

The second of the factors underlying the normal electrocardiogram is the *sequence of contraction* of the chambers. Disturbance may occur in the regular succession of the activity of the pace-maker, as in sinus irregularity (Fig. 13), or disturbance of sequence may occur between the pace-maker (the sinus node) and the auricles, as in sino-auricular block (Fig. 14). Disturbance in sequence occurs also between the auricles and the ventricles (Figs. 15 and 16).<sup>11</sup> These are the familiar heart-blocks, and as rhythmic disturbances require no special description from the electrocardiographic point of view. But certain details of the ventricular mechanism in complete auriculoventricular dissociation have been brought to light

by this method. I cite a unique instance. In a case of complete heart-block the nature of the ventricular activity changed for a

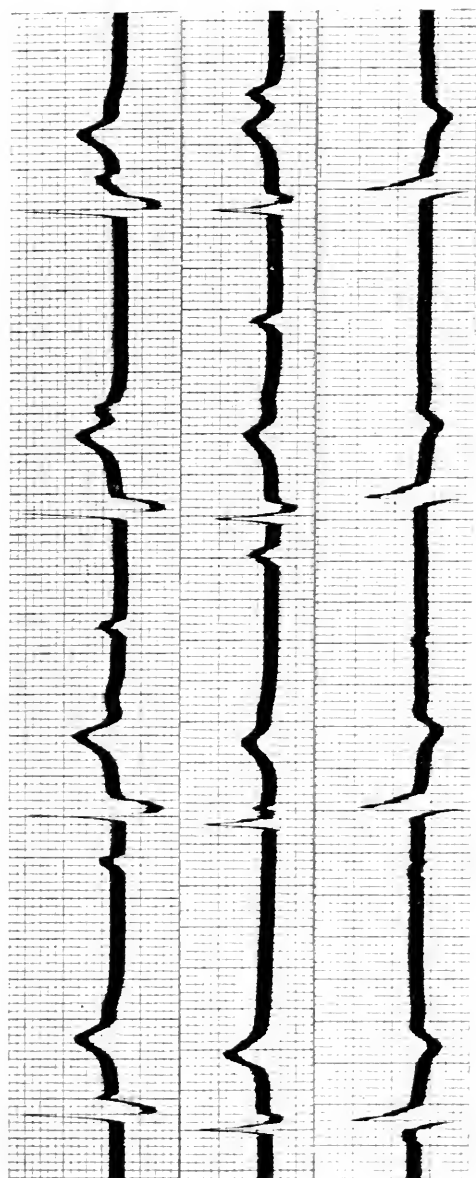


FIG. 16.—Complete auriculoventricular dissociation. Leads 1, 2, and 3. The varying relationship of the *P* waves to the ventricular complexes is shown in many phases.

time in an extraordinary manner. It was first of one form (Fig. 17, *A*) and then of another (Fig. 17, *B*). Electrocardiograms like this

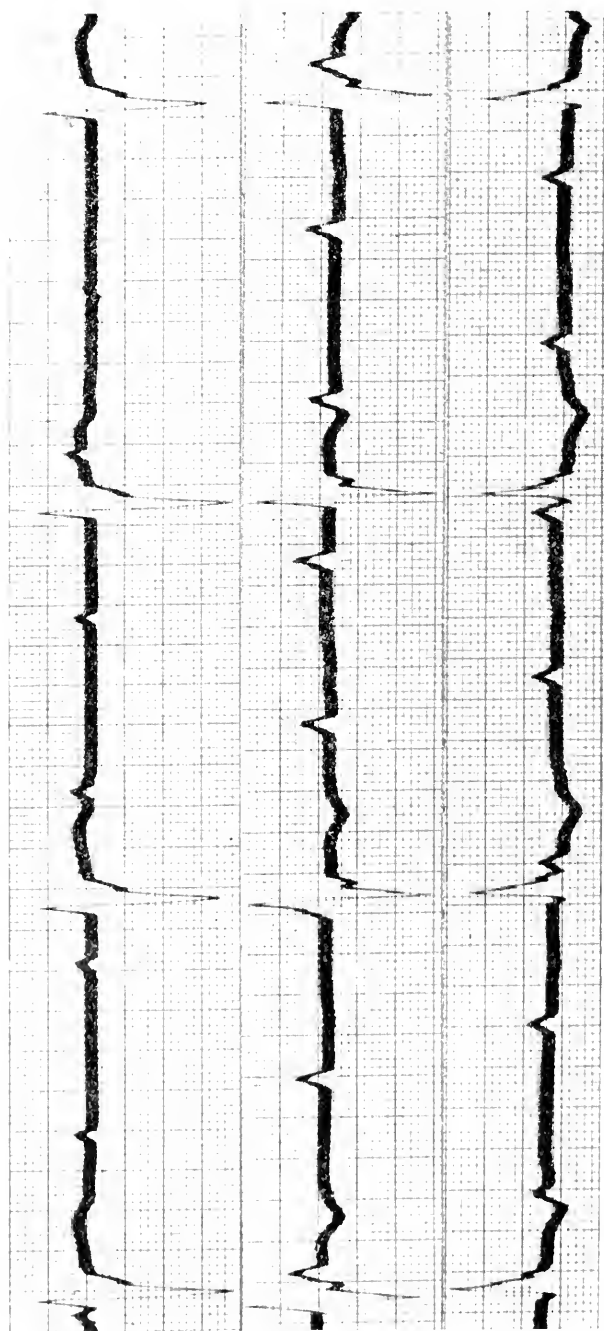


FIG. 17 A.—Complete auriculoventricular dissociation. Leads 1, 2, and 3. The ventricular impulses arise in wall of the right ventricle.

suggest that under circumstances not completely understood, one part and then another of the conduction system is rendered impassable. If the electrocardiogram returns to a former shape

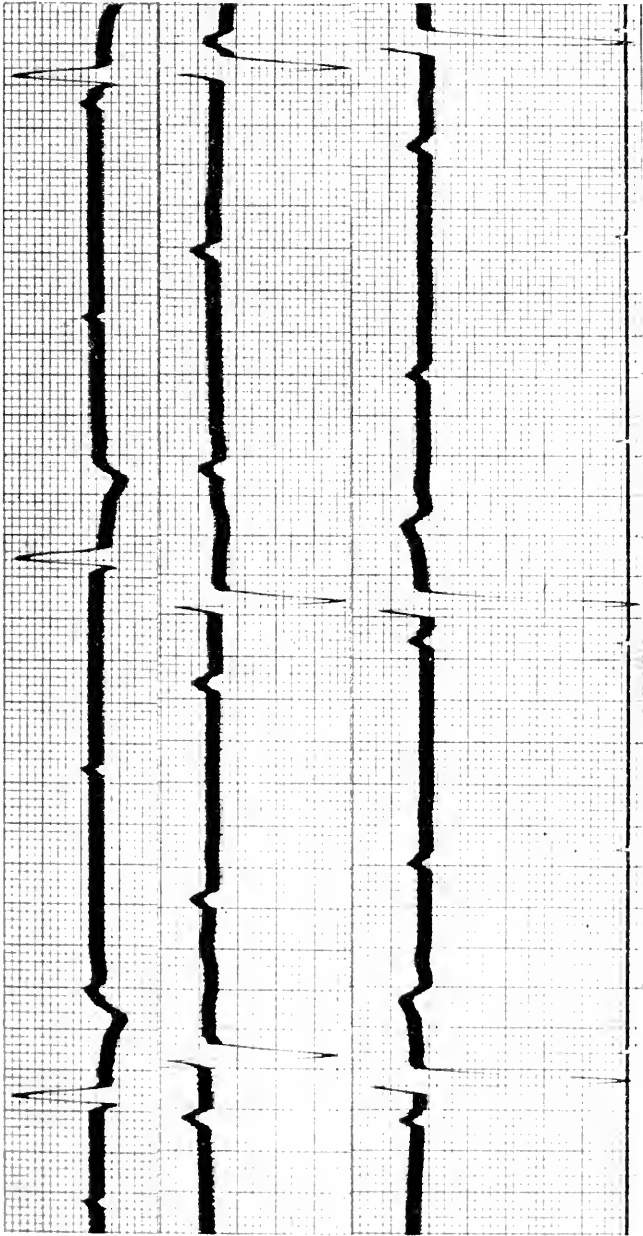


FIG. 17 B.—From the same patient. Leads 1, 2, and 3. The ventricular impulses arise in the wall of the left ventricle.

the cause must have been temporary, as in our case. If it does not, the cause is permanent and is probably an anatomical lesion. When the lesion involves one main branch of the *A-I* bundle, the left branch, for instance, a ventricular electrocardiogram results, having a form similar to that which occurs when the impulses spread from the right ventricle (Fig. 17, *A*). When, on the other hand, the right branch is injured the ventricular electrocardiogram is like that which occurs when the impulses spread from the left ventricle (Fig. 17, *B*). More recently electrocardiograms have been collected which, it is supposed, indicate that the main branches or small subdivisions

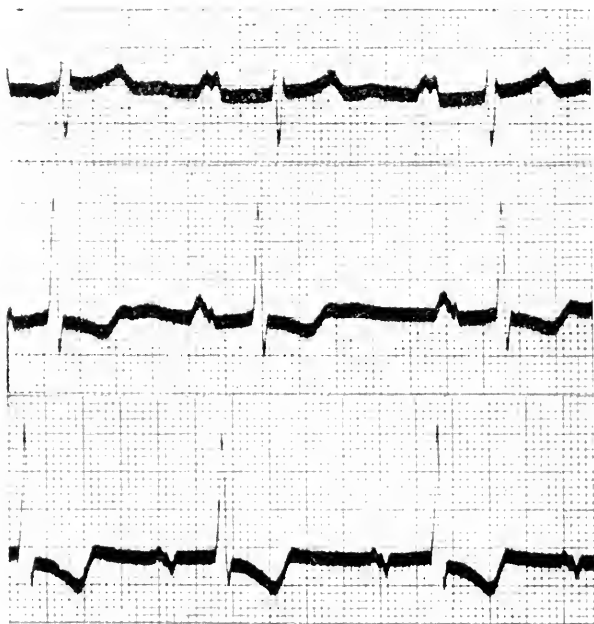


FIG. 18.—Long intervals between the *P* and *R* waves. Leads 1, 2, and 3. In *L*<sub>1</sub> in the first cycle the interval is 0.4 second. The patient was under the influence of digitalis.

of the bundle have received an injury. The recognition of these complicated forms has become commonplace since the introduction of the electrocardiographic method.<sup>12</sup>

Simpler defects in coordination between the auricles and ventricles also occur. The interval between the contraction of the two may be lengthened (Fig. 18). But a more interesting form is that in which the interval is shortened and may be changing. A common, not necessarily fixed, focus in the junctional tissue provides impulses which are conveyed upward to the auricles and downward to the ventricles. The impulses may reach both synchronously, the cases

of true nodal rhythm,<sup>13</sup> or may reach one before the other, or may reach them in an irregular fashion. In the latter event the length of the interval between auricular and ventricular contractions varies (Fig. 6). The mechanism then involves not only disturbance in sequence but also dislocation of impulse formation.

The third factor involved in the production of the normal electrocardiogram is the orderly *coördination of the muscular mass* composing each pair of cavities. The simplest form of disturbance of this mechanism occurs when the form of the auricular (*P*) wave is not rounded above but is split.<sup>14</sup> The two peaks are separated by a deep interval; sometimes the foot-points of the wave are widely separated (Fig. 18). This change has been associated with mitral stenosis, though it is impossible to say that it may not be found

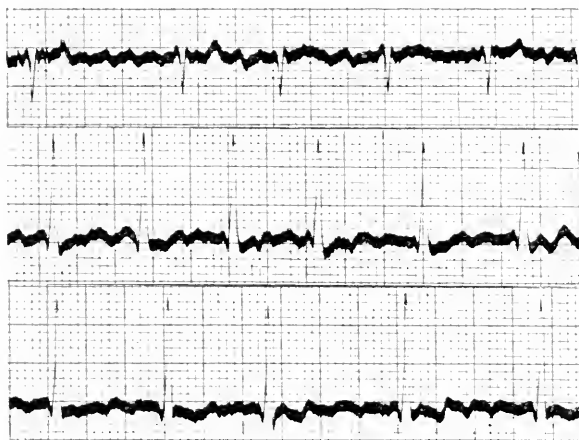


FIG. 19.—Fibrillation of the auricles. Leads 1, 2, and 3. Both fine and coarse waves are seen in the diastolic period.

under other circumstances,<sup>15</sup> and has been supposed to depend on a succession in time of the activity of the two auricles as the result of the mitral lesion.

The extreme example of incoördination in the auricles is seen in the completely irregular pulse which is now known to be due to fibrillation of the auricles (Fig. 19). Rothberger and Winterberg and Lewis<sup>16</sup> established this association by their electrocardiographic studies in 1909. The diagnosis of this rhythm is extremely important for it often furnishes the basis of satisfactory treatment not only in ordinary heart failure but in heart failure occurring in pneumonia and probably in other infections.

Flutter<sup>17</sup> (Fig. 20) is another condition which disturbs the orderly beating of the auricles. Its exact mechanism is still unknown, but its significance and treatment is like that of fibrillation. Its

detection is more difficult than that of fibrillation because occasionally the pulse remains quite regular. Like fibrillation, it may lead to heart failure on account of the resulting rapid rate of the ventricles. Making the diagnosis is important because treatment is often followed by the same satisfactory result as in fibrillation. The diagnosis may be made by other than the electrical method, but it is difficult and uncertain. It occurs spontaneously in pneumonia just as does fibrillation, and then gives rise to the same clinical state, and is controlled in the same way.

The failure of orderly coördination of the muscular mass within the ventricles is very much rarer than in the auricles. Two varieties have been described, and both can be detected only by the electro-



FIG. 20. Flutter of the auricles. Leads 1, 2, and 3. Regularly recurring auricular representatives at the rate of 360 per minute are seen.

cardiogram. The first is associated with the sort of asynchronism between the two ventricles which, v. Leyden supposed, causes a split in the first sound.<sup>12</sup> Experiments and clinical observations have shown that this occurs in bundle branch lesions. I have already included the electrocardiographic signs of this condition, under disturbances in conduction, where it properly belongs. It is mentioned here because ventricular asynchronism which probably causes the split first sound results from the bundle defect.

A failure of orderly coördination resembling auricular fibrillation also occurs in the ventricles.<sup>13</sup> Its occurrence terminates life. That it is a method of death was suggested by Cushny, but the first genuine record of its occurrence was obtained by Robinson. There



is reason to believe that the onset of this rhythm is responsible for many cases of sudden death, especially in aortic insufficiency.

The fourth factor involved in the production of the normal electrocardiogram is the normal *volume and the usual arrangement* of the muscular mass in each pair of cavities. When these are disturbed, hypertrophy or destruction of the walls of the heart or dilatation of its cavities has taken place, or its position in the chest has altered. These abnormalities undoubtedly cause changes in the electrocardiogram (Fig. 21, *A* and *B*), but a correlation between the change in the heart and the change in the electrocardiogram has not yet been satisfactorily made. We are not in possession of the facts which are necessary before a solution of the problem is possible. Originally<sup>19</sup> electrocardiographic changes were believed to indicate corresponding anatomical alterations, but the electrocardiogram is no longer credited with giving that information. The difficulty has arisen because the electrocardiogram, although it sometimes shows the changes which the roentgenogram leads one to expect, does not *always* do so. The state of the matter is as follows: When the right side of the heart is enlarged, as in mitral stenosis, the ordinary three leads<sup>20</sup> yield ventricular curves, the spike of which is down in  $L_1$  and up in  $L_3$  (Fig. 21, *A*). When the left side of the heart is enlarged, as in aortic insufficiency, the ordinary three leads yield ventricular curves, the spike of which is up in  $L_1$  and down in  $L_3$ , and often in  $L_2$  (Fig. 21, *B*). In young children,<sup>21</sup> where the walls of the right side of the heart are relatively large, the curves resemble those of ordinary right-sided enlargement. In cases of congenital<sup>22</sup> cardiac defects, the curves of some resemble preponderant enlargement of one side, the curves of others of the other side. So far the situation is satisfactory, but there are many cases in which we find, for instance, apparently greater left-sided enlargement but fail to find evidence of this in the electrocardiogram. The curves may even be like those seen in right-sided preponderance. The difficulty probably lies in a failure to appreciate what information it is that the electrocardiographic method yields. It does not give an account of the distribution of the muscular mass, but an account of its electrical state. The same arrangement of the mass of the muscle should, and probably always does, give a curve of the same sort. If it does not, the arrangement of the muscle is probably not precisely that which it is believed to be. When it is remembered that knowledge of cardiac hypertrophy is limited, and that enlargement is usually taken to mean size in terms of the Roentgen-ray appearance, and not in terms of the complicated muscle layers and systems of the heart, it is clear why misapprehensions arise. The muscle layers of the heart are, in fact, not coextensive with a single cavity. They probably are strained and injured differently in different valve lesions, and the variations probably determine the shape, size, and constitution of the layers. The altered layers

balances and their electrical equivalents in view, may lead to a solution of the difficulty.

Alterations of the topography of the heart in the chest, due to displacements resulting from accumulations of fluid or air in the pleura or to dislocations resulting from adhesions, are responsible for changes in the electrocardiogram as yet ill defined.<sup>23</sup> Transposition of the heart (dextrocardia)<sup>24</sup> is readily distinguished from displacements by this method. The electrocardiogram, lead for lead, is reversed; to be normal the usual first lead must be taken

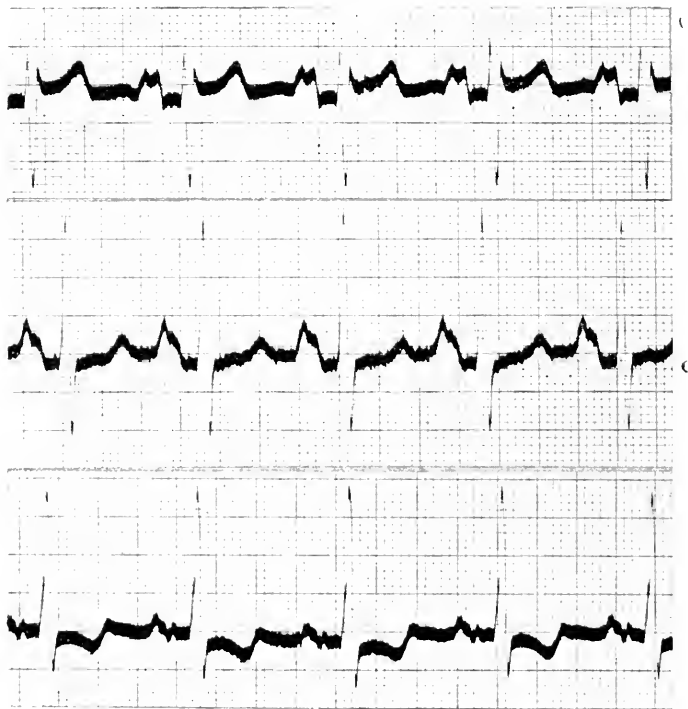


FIG. 21 A.—Curves from a case of mitral stenosis. Leads 1, 2, and 3. Split *P* waves are seen in the three leads; the foot-points of these waves are widely separated. There are short *R* and deep *S* waves in  $I_1$ ; in  $I_2$  and  $I_3$  the *R* waves are tall and the *S* waves short.

from left arm to right arm; the second lead from left arm to right leg; the third lead from right arm to right leg.

The galvanometric method has also been used for recording heart sounds.<sup>25</sup> These have been registered by this method better than by any other so far used. The record is especially valuable when it is combined with the electrocardiogram by means of a two-string galvanometer or by a second instrument. It is unnecessary to describe the method or its results in detail. It has illuminated a

number of questions which have been of interest in auscultation, especially in relation to the auricular systolic murmur in mitral stenosis and its fate when the auricles fibrillate. It has illuminated these questions, but it has contributed nothing new in principle.

It was anticipated, unwisely, that the method would also contribute toward an estimation of the work power of the heart, of its functional efficiency. From this point of view, electrocardiography has been disappointing. But the development of electrical potential, of which the galvanometric method gives information, is only one of the functions of muscular activity. An account of a single function may, naturally, on occasion, be an index of the entire activity

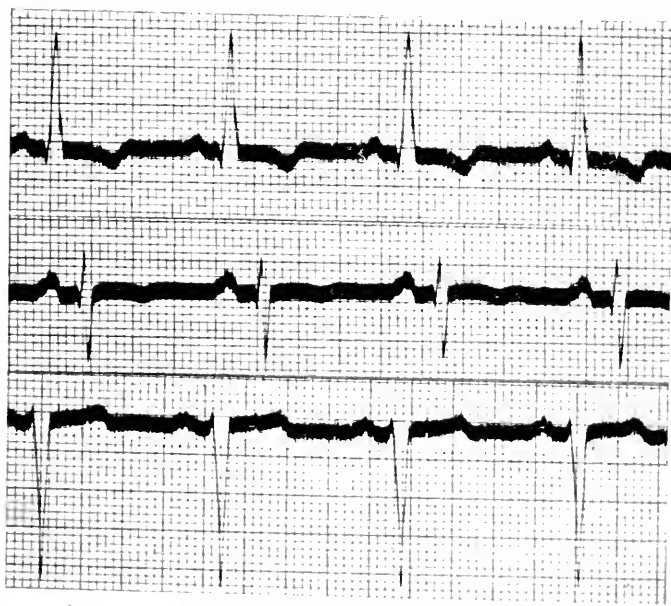


FIG. 21 B.—Curves from a case of cardiosclerosis. In  $L_1$  there are tall  $R$  waves. In  $L_2$  the  $R$  waves are shorter and moderate-sized  $S$  waves appear. In  $L_3$  there are small  $R$  waves but deep  $S$  waves.

of a tissue. But the estimation of electrical discharge has so far not been such an indicator. More detailed observation and closer analysis may indicate capacities which are not yet appreciated.

The description of the normal electrocardiogram and its principal alterations observed in clinical medicine is thus concluded. When the subjects reviewed are grouped under the topics familiar in cardiac pathology, they are seen to be included under headings of irregularities in mechanism, hypertrophy and dilatation, and mal- one may easily believe, alter the electrical values with which we are immediately concerned. Investigations, keeping these muscular

positions and displacements. To these subjects the method has yielded added information. We are now able to think of mechanism in greater detail, as in fibrillation and flutter. Asynchronism of the chambers can now probably be demonstrated. The exact origin and method of the passage of impulses has become a matter of importance, as in paroxysms of tachycardia. In the detailed study of individual waves, notice is taken of alterations which are of consequence in treatment, as in the *T* wave changes arising under the influence of digitalis. In recognizing the value of small alterations of this kind it has become clear that each change in the electrocardiogram may be a change of significance, and may not be dismissed as of no importance.

I have in this review collected data which may be grouped under four headings: (1) those relating to arrhythmias, the mechanism of which has been brought to light by the electrical method; (2) certain facts relating to the *passage of impulses* through the auricles and ventricles, a knowledge of which is being increasingly valuable in diagnosis and in treatment; and (3) certain considerations in regard to the *size* of the heart and (4) its position in the chest.

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## THE OCCURRENCE OF MILIARY TUBERCULOSIS OF THE LIVER IN THE COURSE OF PULMONARY TUBERCULOSIS.

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I HAVE recently made a study of a series of autopsy reports, giving the records of the findings in 131 cases of pulmonary tuberculosis. The object of the investigation was primarily to observe

certain points of interest regarding the tuberculous involvement of the liver and other abdominal organs. Chronic tuberculosis of the liver with large masses of tuberculous material occurs commonly in certain animals, and a few cases have been reported in human beings; but this condition is so rare in man that it is considered as a pathological curiosity, and need not be considered in this discussion.

There is no dearth of literature regarding the frequency of occurrence of tuberculosis in the liver. Ullom's<sup>1</sup> article covers the subject with thoroughness, and Rolleston<sup>2</sup> gives an up-to-date *résumé* of the subject, with references. White<sup>3</sup> has discussed thoroughly the occurrence of miliary tubercles in the liver in the cases studied by him.

It is generally recognized that the liver is involved by miliary tuberculosis in a large percentage of fatal cases, Rolleston putting the figures at about 50 per cent. and White as high as 80 per cent. The opinion of most authors leads us to believe that an involvement of the liver by a tuberculous process is a matter of little importance, and that for some reason it is likely to occur just before death. This view, which seems to be expressed by most writers on the subject, is far from satisfying. I am not aware that I have ever seen an explanation as to why a widespread miliary tuberculosis should occur just before death in the liver, though it does not develop in other organs which ordinarily do not show tuberculous formation, as the pancreas. Tubercle bacilli have been demonstrated in the bile, and they must be passed through the liver, more or less constantly, or deposited in its spaces throughout the course of chronic pulmonary disease.

Much work has been done on the question of the effect of tubercle bacillus in the production of fibrosis of the liver, and it seems probable, as held by Stoerck and others,<sup>4</sup> and as confirmed by the observance of Lvenson and Karsner,<sup>5</sup> that a gradual infection of the liver can take place with a disappearance of the tubercles as formed, resulting in a periportal fibrosis. This does not, however, in any way explain the facts found at autopsy, where we find, as a rule, a wide distribution of young miliary tubercles of approximately the same age, seeming to indicate an overwhelming infection. It would seem necessary to consider whether this condition can exist without serious result.

The following points have been observed: In the liver, miliary tuberculosis is usually demonstrable microscopically, the tubercles fairly young in state of development and occurring in the peri-

<sup>1</sup> Amer. Jour. Med. Sci., 1909, cxxxvii, 691.

<sup>2</sup> Diseases of the Liver, Gall-bladder, and Bile Ducts, London, 1912, 2d ed.

<sup>3</sup> Fifth Annual Report of the Henry Phipps Institute, Philadelphia, 1909.

<sup>4</sup> Wien. klin. Wchnschr., 1907, xx, 817.

<sup>5</sup> Univ. Penna. Med. Bull., Philadelphia, 1909, xxii, 167.

lobular spaces, about the portal vessels, with the greatest frequency. The tubercles are usually not demonstrable grossly, unless there is present a miliary tuberculous peritonitis with invasion of the liver capsule. There may be perilobular fibrosis, and there is likely to be considerable degree of fatty change. In the kidney, tubercles are seen grossly in a much larger proportion of cases than they are found in histological examination, as noted by White. Occasionally old lesions may be seen on the kidney, either caseous or fibrous, or perhaps a single young tubercle; but in histological sections cut for the purpose of examining the kidney structure a tubercle has very seldom been encountered. In the spleen they are found much more frequently than in the kidney, and in the spleen they are older, as a rule, than in the liver. It is impossible to say just how old these gray tubercles found in the liver are, but in working with rabbits, Evans, Bowman, and Winternitz,<sup>6</sup> in studying the pathogenesis of the tubercle of the giant cell in experimental tuberculosis, find a beginning of tubercle formation within six hours after injection of the bacilli into the mesenteric vein and well-developed tubercles within forty-eight hours.

The 131 cases studied in this series have been divided into four classes:

Class A.—Cases apparently dying of pulmonary tuberculosis, showing miliary tubercles of the liver; these are, as nearly as can be determined from the autopsy records, and in some cases from a study of clinical histories, cases which may properly be said to have died from pulmonary involvement, that is, not dying from such intercurrent causes, as violent hemorrhage, advanced amyloid disease, severe pneumonia with acute consolidation of the lung tissue, etc. These cases all show miliary tuberculosis microscopically, but in comparatively few it is demonstrable grossly.

Class C.—These are cases which would be diagnosed at autopsy as more or less generalized miliary tuberculosis, usually showing miliary tubercles of the peritoneum, and possibly of the meninges, spleen, liver, and perhaps of the bladder; but here particularly are found cases of omental and peritoneal involvement, in which it seems that a spread to the liver by way of the lymphatics of the capsule has taken place. A marked point of difference between this class and the first is that in these cases the miliary tuberculosis present in the liver is nearly always recognized grossly. These cases all show miliary tuberculosis of the liver.

Class D.—These are cases of advanced tuberculosis where death is due to some intercurrent event, as acute cardiac dilatation, acute pneumonia, etc. (In this is included tuberculous pneumonia, where consolidation of both lungs is almost complete.) These cases do not show miliary tubercles of the liver.

<sup>6</sup> Jour. Exper. Med., 1914, xix, 283.

Class X.—These are cases apparently dying from pulmonary tuberculosis in which tubercles were not reported on histological examination. It is difficult to classify these cases, but we feel that on the average it has been done fairly. There are probably several cases under "C" which really belong in classification "A," and there are some cases under "X" which should probably be placed in "D." Mention should be made of the question of tuberculous pneumonia, in which there was consolidation of nearly all of the lung tissue. This was considered as the cause of death under classification "D," but considerable degrees of consolidation, if of a tuberculous nature, have been classified under "A" or "X."

A summary of the results show: "A," 49 cases; "D," 29 cases; "C," 33 cases; and "X," 20 cases. Eighty-two cases, or about 63 per cent., therefore, showed miliary tuberculosis of the liver. What appears more significant, however, is that the 29 cases classed under "D," all of which showed active pulmonary tuberculosis, but with death from independent causes, or as the result of acute complications, none showed miliary tubercles in the liver. This is the point, suggested by this compilation, which demands explanation. It would seem that the liver can take care of a gradual tuberculous infection, but that a sudden and overpowering infection of the portal circulation overwhelms the liver resistance, and there ensues a sudden development of disseminated miliary tuberculosis. It is reasonable to assume that this must have a profound constitutional effect, and in the case of an individual weakened by a long course of chronic disease, this might readily lead to a fatal result.

Infection of the portal circulation may take place either from the intestines, which are nearly always infected, or from the spleen. Mechanically the ideal source of a massive infection of the portal stream lies in the spleen, in which the tubercles are apt to be comparatively large, of varying age, and lying in close relation to large blood spaces leading directly into the portal stream.

While it is unsafe to draw parallels between human tuberculosis and experimental tuberculosis in animals, the work of Lewis and Margot,<sup>7</sup> showing an apparent increase in resistance to tuberculosis after the removal of the spleen in mice, suggests that the spleen may be a source of infection to the liver.

There is need for considerable research work to determine the part played by the liver in fatal tuberculosis. If this series of cases is representative, and if, as a rule, these findings are present, viz., that in cases dying from pulmonary tuberculosis there is usually present a wide-spread miliary tuberculosis of apparently recent onset, and in cases dying from other causes this is not found, we must consider two possible explanations for these findings: (1) that in cases dying from tuberculosis the liver tissue, for some



reason, loses its resistance to the tubercle bacilli shortly before death, and at the same time is freely infected through the portal circulation, or (2) that in these cases the liver is able to cope with a gradual infection, but a sudden and overwhelming flooding of the portal stream with the tubercle bacilli overpowers the hepatic resistance, allowing tubercles to develop, and that the reaction in the liver has a severe constitutional effect, often determining the fatal issue.

In view of the fact that we do not find miliary tuberculosis developing in the liver in cases of active tuberculosis dying from independent causes, and that other tissues of the body are not rendered susceptible to tubercle development with the liver as death approaches, the latter explanation seems more reasonable than the former. I think it probable that such infection takes place by way of the portal circulation, and probably very frequently from the spleen. This view accords, in a measure, with the observation that experimentally the development of fatal tuberculosis is delayed by the removal of the spleen.

I desire to express my sincere appreciation to Prof. Allen J. Smith, of the University of Pennsylvania, both for valuable suggestions and for placing at my disposal the autopsy records of the Pathological Department of the University, and to Dr. H. R. M. Landis, director of the Phipps Institute of the University of Pennsylvania, for allowing me to refer to the autopsy records of that institute.

Cases apparently dying of pulmonary tuberculosis and showing miliary tuberculosis of the liver on microscopic examination:

## CLASS A.

1900—	26	
	34	
	54	
	35	Tuberculous pneumonia.
1901—	64	
	86	
	91	
	107	
1902		
(?) —	5	Pneumonia and disseminated tuberculosis.
	73	
1903		
(?) —	12	Locomotor ataxia.
1904—	15	
	24	
	26	
	35	
	37	
	66	Miliary tuberculosis of lungs and pneumonia.
	79	
	98	Tuberculous pneumonia.
	120	
	132	
	157	
	158	
	202	Tuberculous pneumonia.

Balance		CLASS A (Continued).
forward—	24	
1905—	1	Acute parenchymatous nephritis.
	6	Tuberculous pneumonia; endocarditis (mitral).
	27	Hemiplegia; amyloid; tuberculous pneumonia.
	90	
	108	
	112	
	123	
	138	
	157	
	4659	
	4587	
	4522	
	4500	
	1462	
	4460	
	4380	
	4306	
	4281	
	4282	
	4272	
	4248	Recent hemorrhage, eight ounces.
	1232	Chronic advanced pulmonary tuberculosis. At right base there is pneumonic consolidation, but no microscopic examination of lungs (pneumonia ?).
	4198	Also amyloid liver and spleen.
	4155	
	4148	Hypernephroma of kidney, but thoroughly encapsulated and no metastasis.
<hr/>		
49 cases.		

Cases of more or less generalized tuberculosis, usually showing involvement of peritoneum and omentum, or of general miliary tuberculosis. All show miliary tuberculosis of the liver:

		CLASS C.
1900 —	61	Balance forward— 18
1901 —	28	1904— 112
	114	170
	124	174
	214	190
	220	196
1902 —	6	213
	75	1905— 3
	191	9
	212	46
	215	47
1903 —	152	49
1904 —	9	69
	17	110
	63	126
	110	140
	117	—
	131	33 cases.

Cases of pulmonary tuberculosis dying from other causes and not showing miliary tuberculosis of the liver on microscopic examination:

## CLASS D.

- 1900— 55 Advanced amyloid, aortic, and mitral valvulitis (veg.), hydro-pericardium; tuberculosis (primary); epididymitis and scrotum.
- 1901— 48 Ulcer of stomach and hemorrhage into pancreas; chronic and  
154 acute miliary pulmonary tuberculosis, and abscess; perforation of esophagus.
- 1902— 15 Rheumatoid arthritis; advanced amylosis of liver, kidney, spleen, etc.  
16 Diabetes; pulmonary gangrene.  
30 Chronic pulmonary tuberculosis; acute bronchopneumonia; acute infiltrated liver; portal space infiltrated.
- (?) 65 Cancer of bowels; edema of lungs (?); tuberculous ulcer; mesenteric nodes.  
182 Pyelonephritic tuberculosis; subacute fibroid pleurisy; edema of brain (?); tuberculosis (?).  
202 Psoas abscess; miliary tuberculosis of lungs; chronic mitral valvulitis; pulmonary hemorrhage.
- 1903— 42 Pulmonary tuberculosis; pneumonia.  
154 Acute dilatation of heart following operation of glands of neck.
- 1904— 6 Nephritis; dropsy; operation for decapsulation; pulmonary fibrosis and fibroid tubercles.  
18 Operation on tuberculous shoulder-joint followed by miliary tuberculosis of lungs and bronchopneumonia.  
86 Tuberculous meningitis; internal hydrocephalus.  
105 Tuberculous pneumonia; complete of right and almost complete consolidation of left.  
147 Cardiac hypertrophy; valvulitis; bronchopneumonia; tuberculosis.  
171 Hypertrophy and dilatation of heart; hydropericardium; tuberculous pneumonia.  
184 Fibroid tuberculosis of left lung; miliary tuberculosis of right lung; edema and congestion; mitral and aortic disease; nephritis.  
187 Myocarditis; acute endocarditis; chronic bronchitis; both apices.
- (X) ? 216 Fibroid and fatty heart; calcified aortic leaflets.  
233 Septicemia; peritonitis.
- 1905— 15 Amyloid spleen, liver, kidney; carcinoma of uterus and kidney.  
(X) 26 Tuberculous pneumonia; tuberculous spleen; pyothorax. (One liter of pus.)  
44 Tuberculous vertebrae; amyloid liver, kidney, and spleen—advanced.  
64 Pulmonary tuberculosis; tuberculous pneumonia; pulmonary congestion; brown atrophy of heart; chronic nephritis. Aged eighty years; tuberculous spleen.  
106 Miliary tuberculosis of lungs and peritoneum; acute nephritis; death following operation on ileum and sigmoid; no tubercles in spleen.  
159 Empyema; collapse of lung; cloudy swelling of kidney; tuberculous kidney and spleen.  
4364 Tuberculous pneumonia, acute; both lungs practically solid.  
4243 Acute pneumonia; sudden death.

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29 cases.

Cases in which death seems to be a result of pulmonary tuberculosis and which do not show miliary tuberculosis of the liver on microscopic examination:

## CLASS X.

- 1901— 5 Apparently pulmonary tuberculosis, but also edema of brain and gelatinous pneumonia. (Microscopic.)  
 36 Fatty and parenchymatous degeneration of liver.  
 103  
 117  
 1904— 42 Tuberculous meningitis (miliary tubercles).  
 100 Acute parenchymatous nephritis.  
 116 Cardiac fibrosis; bronchopneumonia.  
 120 Myocarditis, fibrosis, and fatty infiltration.  
 176 Brown atrophy of heart; fibroid lung (left); ulcerative tuberculosis of right lung.  
 1905— 13 Chronic myocarditis; chronic diffuse nephritis.  
 33 Tuberculous pneumonia.  
 36 Nephritis; myocarditis; pulmonary edema and congestion.  
 135 Tuberculous pneumonia of right lung (1120 grams), entirely solid; left, slight.  
 4115 Pathological diagnosis written by pathologist personally states miliary tuberculosis of liver; detailed report does not state.  
 4345 Amyloid liver, spleen, kidney, intestines, etc.  
 4287 Few tubercles grossly. Not reported microscopically.  
 4224 Typical course of chronic pulmonary tuberculosis; tuberculosis in liver reported grossly, but not mentioned in histological report.  
 4197 Same as 4224. Reported grossly.  
 4221  
 4316

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20 cases.

## ANALYSIS OF ONE HUNDRED AND THIRTY-FOUR CASES OF BACTERIEMIA.

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EXCEPTING the statements in the monographs of Canon<sup>1</sup> and Lenhartz,<sup>2</sup> and the brief summaries of Soper,<sup>3</sup> Jochmann,<sup>4</sup> Burnham,<sup>5</sup> Bertelsmann,<sup>6</sup> and a few others, it is difficult to find statistics of volume sufficient to have value in judging the prognosis of bacteriemias. Bertelsmann summarizes 49 cases of bacteriemia, Canon 98, Lenhartz 90, Soper 29, Burnham 111.

In the study here presented we have tabulated 134 cases of

<sup>1</sup> Die Bacteriologie des Blutes bei Infektionskrankheiten, Jena, 1905.

<sup>2</sup> Die septischen Erkrankungen, Nothnagel, Spez. Path. and Therap., Wein., 1903, iii, 1, 1, 197.

<sup>3</sup> A Series of Cases of Staphylococcus aureus sepsis, Proc. New York Path. Soc., 1912, N. S., xii, 223-225.

<sup>4</sup> Handbuch der inn. Med., 1911, i, 655.

Vaccine and Serum Therapy in Septicemia, Ann. of Surg., 1914, lix, 5, 653.

<sup>5</sup> Die Allgemein Infektion bei chirurgischen Infektionskrankheiten, Deutsch. Ztschr. f. Chir., 1901, lxxii, 209.

bacteriemia observed in the various services of the Roosevelt Hospital during the past five years. There are recorded in the briefest possible way. The hospital case number, the age of the patient, the diagnosis, the maximum temperature, the leukocyte count and polymuclear percentage, the bacteriological blood findings, the treatment, and the result are given.

STATEMENT OF LABORATORY METHODS. So far as possible the number of colonies which developed in a poured agar plate from approximately 1 c.c. of blood is entered under the caption blood culture. The result is otherwise indicated as No growth in solid media, Fluid media only used, or Number not noted. From this one gains some knowledge of the grade of bacteriemia represented by the viable organisms present per c.c. in the circulating blood at the time of culture.

We have found the following to be a satisfactory method for routine use; 2 or 3 c.c. of blood are delivered into a French square bottle of a half-pint capacity containing 75 c.c. of infusion broth (acid +0.6); 5 to 6 c.c. into the same type of bottle of one pint capacity containing 200 c.c. of broth of like character, and 1 to 2 c.c. are poured into a Petri plate with 6 to 8 c.c. of agar (acid +0.6) melted and cooked to 42° to 45° C. In many instances additional media were used, including glucose agar and glucose broth with and without the addition of serum or ascitic fluid, glycerin agar, and broth media; also media of varying acidity. At times a portion of blood for examination was treated by one or more of the following means before cultivation: (1) defibrination, (2) allowing coagulation to take place and pouring off the serum, (3) decalcification with potassium oxalate or sodium citrate, (4) laking with distilled water, (5) collection into a flask containing crystal salt enough to make about a 5 per cent. solution of salt in the blood added.

It is unnecessary to make any remarks on the bacteriological classification of the cases other than those of the *Streptococcus* group. Under *Streptococcus hemolyticus* are included 26 cases in which the organism in question was a Gram-positive streptococcus whose colonies in blood agar presented a typical zone of clear hemolysis; and cases Nos. 24, 28, and 104 (all pelvic sepsis); case No. 47 an atypical streptococcus producing diffuse hemolysis and recorded as being dissolved by bile; case No. 14 a conglomerate streptococcus with slight hemolytic activity.

Under *Streptococcus viridans* are included as follows:

I. A Gram-positive diplo- or streptococcus the colonies of which in blood agar show the characteristic green color and are surrounded by a narrow pale green halo. This coccus is not dissolved by bile; in all, 26 cases.

II. Cases 68, 71, 74, 105, 106, as Group I, except that the colonies in blood agar were of a brownish or indifferent color. Case 121 where no growth in blood agar was obtained (here absence of laking

of the red blood cells and diffusion of hemoglobin through the blood-broth mixture would distinguish this growth from that of a typical hemolytic streptococcus).

III. In cases 2, 17, 18, 29, 43, 69 the records are insufficient and the bacteriological diagnosis is made from the clinical type of case.

IV. In cases 26, 39, 129 no bile test was made, otherwise as Group I.

V. Case 73, as Group I, but there is a note of the coccus having been dissolved by bile.

Among these cocci there are only two instances of confusion by means of the bile test. This test as usually performed consisted in the addition of an equal quantity of ox-bile to a convenient amount of a fine suspension of the organism in normal saline. The reaction is quantitative rather than qualitative as a method of differentiating the pneumococcus from the viridans; there are strains of the latter which are dissolved by bile if a relatively large amount of bile is used. The test should be confirmed on several secondary blood agar plants if inconclusive.

Other morphological and cultural characteristics of Gram-positive diplococci are of value in differentiation, especially the presence of capsules; the precipitation of glucose ascitic agar; and the fermentation of inulin, but a classification of the diplococci analyzed in this report by means of any one of these attributes would make a very different list.

So far as animal inoculation is concerned 7 per cent. (cases Nos. 15, 21, 25, 105, 127, 129, 130) of the cocci grouped under viridans were tried on the smaller laboratory animals without producing demonstrated lesions. The relative absence of pathogenicity of the viridans is of great aid in grouping certain doubtful strains of diplococci.

In the accompanying table the more common clinical conditions are summarized. It will be noted that no case with endocarditis recovered, that the prognosis of bacteriemia with otitis or with osteomyelitis is relatively good, while 20.4 per cent. of cases of sepsis recovered. Following Jochmann's<sup>7</sup> definition we have included under sepsis those examples of systemic response to the invasion of the blood-stream by pyogenic organisms or their toxins in which the symptoms arising from the blood infection or intoxication stand in the foreground of the clinical picture as distinguished from bacteriemia, which signifies the mere presence of micro-organisms in the blood-stream without reference to symptoms or other conditions.

SUMMARY OF BLOOD COUNTS. In the following are tabulated the average number of leukocytes and the polynuclear percentage

<sup>7</sup> *Loc cit.*

of the fatal and of the recovered cases of the commoner varieties of bacteriemia, with a general summary showing the averages of all cases.

## GENERAL SUMMARY.

Organism.	Number of cases.	Died.	Recovered.	Im-proved.	Unim-proved	Died per cent.
<i>Streptococcus hemolyticus</i>	31	21	7	1	2	67.0
<i>Streptococcus viridans</i>	40	25	10	2	3	64.0
<i>Streptococcus mucosus</i>	1	1				100.0
<i>Staphylococcus aureus</i>	39	22	14	3		56.0
<i>Staphylococcus albus</i>	3	2	1			66.0
<i>Pneumococcus</i>	10	6	2		2	60.0
<i>Bacillus coli</i>	6	4	2			66.0
<i>Bacillus influenzae</i>	2	2				100.0
Anaërobic streptococci	3	2	1			66.0
<i>Bacillus mucosus capsulatus</i>	1	0	1			0
<i>Bacillus mallei</i>	2	2				100.0
<i>Bacillus fecalis alkaligenes</i>	1		1			0
Mixed infection	7	6	1			86.0
<i>Streptococcus hemolyticus</i> and <i>staphylococcus aureus</i>	1	1				100.0
<i>Streptococcus hemolyticus</i> and <i>bacillus typhosus</i>	1	1				100.0
<i>Streptococcus viridans</i> and <i>staphylococcus aureus</i>	1		1			0
<i>Streptococcus viridans</i> and <i>bacillus coli</i>	1	1				100.0
<i>Staphylococcus aureus</i> and <i>bacillus coli</i>	1	1				100.0
<i>Bacillus proteus</i> and <i>bacil-lus coli</i>	1	1				100.0
<i>Bacillus influenzae</i> and <i>sta-phylococcus albus</i>	1	1				100.0
All cases	134	83				61.1

## TABLE OF CLINICAL CONDITIONS.

	Died.	Recovered.	Im-proved.	Unim-proved.	Recovered per cent.
Postpartum infection	10	1		1	9.09
Arthritis	1	4	1		80.0
Endocarditis	22			3	0
Otitis media with or without mas-toiditis	2	4			66.6
Pelvic cellulitis	2				0
Osteomyelitis	5	4	1		44.4
Sepsis	39	10	3	3	20.4

In general the difference in the blood picture in the fatal and non-fatal cases is not striking. In the average of all cases the former show a slightly higher polynuclear percentage and lower total leukocyte count, but there are exceptions in individual groups. In the streptococcus group, for example, the leukocyte counts in fatal and non-fatal cases are approximately the same, while the polynuclear percentage is the reverse of that anticipated. One may conclude that the ordinary leukocyte and differential blood count is of slight value in prognosis of bacteriemias.

Organism.	Fatal cases.		Recovered cases.	
	Leukocytes.	Poly-nuclears, per cent.	Leukocytes.	Poly-nuclears, per cent.
<i>Streptococcus hemolyticus</i>	18,347	81.4	18,742	85.2
<i>Streptococcus viridans</i>	15,976	78.1	17,222	75.1
<i>Streptococcus mucosus</i>				
<i>Staphylococcus aureus</i>	22,822	85.1	15,380	79.5
<i>Staphylococcus albus</i>	22,800	78.0		
<i>Pneumococcus</i>	26,350	86.5	35,900	82.0
<i>Bacillus coli</i>	18,233	79.0	11,400	70.1
<i>Bacillus influenzae</i>				
<i>Anaerobic streptococci</i>	18,000	78.0		
<i>Bacillus mucosus capsulatus</i>			13,800	90.0
<i>Bacillus mallei</i>				
<i>Bacillus fecalis alkaligenes</i>				
Average of all cases	19,877	82.8	17,651	78.3

While it is appreciated that statistics have little value in a series of varied cases such as this, it is of some interest to note the relatively low mortality in the group treated surgically and in the group treated by palliative measures only, and to compare this result with the high mortality in the groups treated by vaccines and sera. Such statistical revelation confirms the impression gained from bedside experience that our present methods of specific therapy of generalized pyogenic infections have not yet established their standing in court.

**SUMMARY AND CONCLUSIONS.** One hundred and thirty-four examples of bacteriemia from a general hospital service are summarized; 61.1 per cent. of these cases recovered. Noteworthy also is the recovery of 20.4 per cent. of the cases of sepsis. The slight value of the ordinary leukocyte and differential count in prognosis of bacteriemias is shown, as is also the futility of present measures of specific therapy of generalized infections.

#### RESULTS OF TREATMENT.

Treatment.	Number of cases.	Died.	Recovered	Improved.	Unimproved.	Died per cent.
Vaccines	25	17	4	2	2	81.0
Transfusion	2	2				100.0
Serum	4	3	1			75.0
Under surgical treatment	17	22	22	3		50.0
Palliative	55	39	11	1	4	65.0

#### STREPTOCOCCUS VIRIDANS—CURED.

CASE No. 88.—*Age*—Thirty-five years. *Diagnosis*—Pulmonary abscess; bacteriemia. *Leukocytes*—21,000; polynuclears, 79 per cent. *Blood culture*—*Streptococcus viridans*, number not noted (abundant); *streptococcus viridans*, few; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 102, D. 5411.—*Age*—Sixteen years. *Diagnosis*—Typhoid fever; phlebitis. *Maximum temperature*—106.4°. *Leuko-*



*cytes*—10,700; polynuclears, 87 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 106, D. 4908.—*Age*—Thirty-four years. *Diagnosis*—Acute articular rheumatism; bacteriemia. *Maximum temperature*—103.2°. *Leukocytes*—19,900; polynuclears, 79 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within a period of several days; no growth in solid media. *Treatment*—Salicylates. *Result*—Cured.

CASE No. 130, A. 1719.—*Age*—Twenty-one years. *Diagnosis*—Chronic arthritis of knee; bacteriemia. *Maximum temperature*—99.2°. *Leukocytes*—13,400; polynuclears, 66 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Salicylates. *Result*—Cured.

CASE No. 127, A. 2253, A. 2623.—*Age*—Fifty years. *Diagnosis*—Adenocarcinoma of breast; metastasis in axillary fat; sepsis. *Maximum temperature*—103°. *Leukocytes*—9400; polynuclears, 56 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within a period of one week; no growth in solid media; subsequent culture negative. *Treatment*—Vaccines. *Result*—Cured.

CASE No. 128, D. 4654.—*Age*—Forty-five years. *Diagnosis*—Sepsis. *Maximum temperature*—105°. *Leukocytes*—24,000; polynuclears, 78 per cent. *Blood culture*—*Streptococcus viridans*; four positive cultures within a period of ten days, from 2 to 9 per c.c. *Treatment*—Palliative. *Result*—Cured.

CASE No. 129, D. 1538.—*Age*—Eighteen years. *Diagnosis*—Subacute arthritis; chronic endocarditis; bacteriemia. *Maximum temperature*—102.6°. *Leukocytes*—20,000; polynuclears, 64 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Salicylates. *Result*—Cured.

CASE No. 74.—*Age*—Sixty years. *Diagnosis*—Bronchitis. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 121, A. 1812.—*Age*—Thirty-one years. *Diagnosis*—Chronic otitis; chronic mastoiditis; chronic appendicitis; bacteriemia. *Maximum temperature*—101°. *Leukocytes*—14,200; polynuclears, 81.5 per cent. *Blood culture*—*Staphylococcus aureus* accompanied by *streptococcus viridans*; no growth in solid media. *Treatment*—Appendectomy. *Result*—Cured.

CASE No. 105, B. 2087.—*Age*—Fourteen years. *Diagnosis*—Acute appendicitis; retrocecal abscess; bacteriemia. *Maximum temperature*—104.6°. *Leukocytes*—22,400; polynuclears, 86 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Incision and drainage of appendicular and subsequent abscess. *Result*—Cured.

## STREPTOCOCCUS VIRIDANS—IMPROVED.

CASE No. 21, 1909, VIII, 1.—*Age*—Twelve years. *Diagnosis*—Sepsis. *Maximum temperature*— $104^{\circ}$ . *Leukocytes*—20,000; polynuclears, 69.5 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media; subsequent cultures negative. *Treatment*—Palliative. *Result*—Improved.

CASE No. 110, E. 360.—*Age*—Thirteen years. *Diagnosis*—Acute articular rheumatism; chronic endocarditis; bacteremia. *Maximum temperature*— $104.4^{\circ}$ . *Leukocytes*—24,300; polynuclears, 74 per cent. *Blood culture*—*Streptococcus viridans*: 1 per c.c. *Treatment*—Thoracentesis; salicylates. *Result*—Improved.

## STREPTOCOCCUS VIRIDANS—UNIMPROVED.

CASE No. 6, D. 4512.—*Diagnosis*—Acute septic endocarditis. *Maximum temperature*— $104^{\circ}$ . *Leukocytes*—11,200; polynuclears 71 per cent. *Blood culture*—*Streptococcus viridans*: 40 per c.c. *Treatment*—Vaccines. *Result*—Unimproved.

CASE 15, D. 1923.—*Age*—Sixteen years. *Diagnosis*—Septic endocarditis. *Maximum temperature*— $101.8^{\circ}$ . *Leukocytes*—20,800; polynuclears, 43.5 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Salicylates. *Result*—Unimproved.

CASE No. 17, D. 446.—*Age*—Twenty-six years. *Diagnosis*—Chronic + acute endocarditis. *Maximum temperature*— $103.8^{\circ}$ . *Leukocytes*—32,000; polynuclears, 91 per cent. *Blood culture*—*Streptococcus viridans*; number of colonies not noted. *Treatment*—Salicylates; vaccines. *Result*—Unimproved.

## STREPTOCOCCUS VIRIDANS—DIED.

CASE No. 1, D. 6482.—*Age*—Twenty-eight years. *Diagnosis*—Sepsis; endocarditis. *Maximum temperature*— $104^{\circ}$ . *Leukocytes*—13,400; polynuclears, 85 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within an interval of a few days; numerous in both colonies. *Treatment*—Palliative. *Result*—Died.

CASE No. 2, D. 6014.—*Age*—Forty years. *Diagnosis*—Acute septic endocarditis. *Maximum temperature*— $106.2^{\circ}$ . *Leukocytes*—19,200; polynuclears, 73 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within an interval of a few days; numerous colonies in second. *Treatment*—Vaccines. *Result*—Died.

CASE No. 4, D. 4698.—*Age*—Thirty-five years. *Diagnosis*—Sepsis; pericarditis. *Maximum temperature*— $100^{\circ}$ . *Leukocytes*—7800; polynuclears, 79 per cent. *Blood culture*—*Streptococcus viridans*; innumerable colonies. *Treatment*—Palliative. *Result*—Died.

CASE No. 7, D. 4359.—*Age*—Fifty-two years. *Diagnosis*—Septic endocarditis. *Maximum temperature*—103°. *Leukocytes*—19,100; polynuclears, 88 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Vaccines. *Result*—Died.

CASE No. 18, D. 243.—*Age*—Twenty years. *Diagnosis*—Sepsis. *Maximum temperature*—105°. *Leukocytes*—33,000; polynuclears, 88.5 per cent. *Blood culture*—*Streptococcus viridans*, number of colonies not noted. *Treatment*—Salicylates; vaccines. *Result*—Died.

CASE No. 20, D. 5054.—*Age*—Sixty-one years. *Diagnosis*—Sepsis. *Maximum temperature*—104.4°. *Leukocytes*—8000; polynuclears, 54 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within an interval of a few days: 1 per c.c. *Treatment*—Salicylates. *Result*—Died.

CASE No. 25, D. 365.—*Diagnosis*—Acute septic endocarditis. *Maximum temperature*—104.6°. *Leukocytes*—11,600; polynuclears, 72 per cent. *Blood culture*—*Streptococcus viridans*; three positive cultures within a period of several days, from 80 to 140 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 26, C. 255, D. 605.—*Age*—Forty-two years. *Diagnosis*—Acute septic endocarditis, hydrosalpinx. *Maximum temperature*—104.2°. *Leukocytes*—18,000; polynuclears, 79 per cent. *Blood culture*—*Streptococcus viridans*; three positive cultures within a period of several days, from 25 to 180 c.c. *Treatment*—Right salpingo-oörophorectomy. *Result*—Died.

CASE No. 30, D. 3695.—*Age*—Twenty-six years. *Diagnosis*—Chronic + acute septic endocarditis. *Maximum temperature*—102.8°. *Leukocytes*—9600; polynuclears, 69 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within a period of a few days; 100 per c.c. in second. *Treatment*—Salicylates. *Result*—Died.

CASE No. 37, C. 2292.—*Age*—Twenty-nine years. *Diagnosis*—Acute diffuse peritonitis; pelvic cellulitis; meningitis; sepsis. *Maximum temperature*—106.6°. *Leukocytes*—19,500; polynuclears, 89 per cent. *Blood culture*—*Streptococcus viridans*: 2 per c.c., and *Bacillus coli* (few). *Treatment*—Palliative. *Result*—Died.

CASE No. 39, D. 5355.—*Diagnosis*—Subacute endocarditis. *Maximum temperature*—102°. *Leukocytes*—13,600; polynuclears, 77 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 40, D. 5726.—*Age*—Twenty years. *Diagnosis*—Sepsis. *Maximum temperature*—104.2°. *Leukocytes*—10,200; polynuclears, 84 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Vaccines. *Result*—Died.

CASE No. 42, D. 6282.—*Diagnosis*—Osteomyelitis of vertebrae; bacteriemia. *Maximum temperature*—103.8°. *Leukocytes*—5600; polynuclears, 72 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 43, D. 1087.—*Age*—Thirty-one years. *Diagnosis*—Acute septic endocarditis. *Maximum temperature*—104°. *Leukocytes*—16,000; polynuclears, 78 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 44, D. 1919.—*Age*—Twenty-three years. *Diagnosis*—Chronic + acute endocarditis. *Maximum temperature*—102.6°. *Leukocytes*—12,000. *Blood cultures*—*Streptococcus viridans*; eight positive cultures within a period of several weeks, from 2 to 70 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 45, D. 3783.—*Age*—Forty-five years. *Diagnosis*—Chronic + acute endocarditis. *Maximum temperature*—104°. *Leukocytes*—13,000; polynuclears, 78 per cent. *Blood cultures*—*Streptococcus viridans*: 4 per c.c. *Treatment*—Vaccine. *Result*—Died.

CASE No. 49, D. 4936.—*Age*—Thirty-one years. *Diagnosis*—Sepsis. *Maximum temperature*—104.6°. *Leukocytes*—10,500; polynuclears, 49 per cent. *Blood culture*—*Streptococcus viridans*; two positive cultures within a period of a few days: 15 per c.c. in first, 300 per c.c. in second. *Treatment*—Transfusion. *Result*—Died.

CASE No. 61.—*Age*—Twenty years. *Diagnosis*—Subacute endocarditis; pyelitis. *Blood culture*—*Streptococcus viridans*, 2 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 68, E. 109, E. 313, E. 420, D. 5084.—*Age*—Ten years. *Diagnosis*—Acute arthritis; sepsis. *Maximum temperature*—104.4°. *Leukocytes*—33,400; polynuclears, 85 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media; culture one month later negative. *Treatment*—Palliative. *Result*—Died.

CASE No. 69.—*Age*—Thirty-five years. *Diagnosis*—Septic endocarditis. *Leukocytes*—24,000; polynuclears, 92 per cent. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Vaccines. *Result*—Died.

CASE No. 29, 1909, X, 12.—*Age*—Thirty years. *Diagnosis*—Septic endocarditis. *Maximum temperature*—106.2°. *Leukocytes*—15,000; polynuclears, 88 per cent. *Blood culture*—*Streptococcus viridans*; three positive cultures within a period of one week; six to twelve colonies per c.c. *Treatment*—Vaccines. *Result*—Died.

CASE No. 70.—*Age*—Sixty years. *Diagnosis*—Chronic + acute endocarditis. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Result*—Died.

CASE No. 71.—*Age*—Twenty years. *Diagnosis*—Sepsis. *Blood culture*—*Streptococcus viridans*; 3 per c.c. *Result*—Died.

CASE No. 73. *Age*—Thirty years. *Diagnosis*—Subacute endocarditis. *Blood culture*—*Streptococcus viridans*; no growth in solid media. *Treatment*—Vaccines. *Result*—Died.

CASE No. 91, D. 1671. *Age*—Thirty-six years. *Diagnosis*—Septic endocarditis. *Maximum temperature*—106°. *Leukocytes*—

23,000; polynuclears, 95 per cent. *Blood culture*—*Streptococcus viridans*; five positive cultures within a period of a week; 3 or 4 per c.c. *Treatment*—Celiotomy; palliative. *Result*—Died.

STREPTOCOCCUS HEMOLYTICUS—CURED.

CASE No. 9, B. 3339.—*Age*—Twenty-eight years. *Diagnosis*—Acute mastoiditis; erysipelas; bacteriemia. *Maximum temperature*—104.8°; *Leukocytes*—22,600; polynuclears, 92 per cent. *Blood culture*—*Streptococcus hemolyticus*; two positive cultures within a period of a few days, from 8 to 16 per c.c. *Treatment*—Mastoidectomy. *Result*—Cured.

CASE No. 19, B. 82.—*Age*—Forty years. *Diagnosis*—Cellulitis of hand and forearm; bacteriemia. *Maximum temperature*—105°. *Leukocytes*—21,000; polynuclears, 81 per cent. *Blood culture*—*Streptococcus hemolyticus*; 4 per c.c. *Treatment*—Multiple incisions. *Result*—Cured.

CASE No. 109, C. 278.—*Age*—Twenty-six years. *Diagnosis*—Pelvic abscess; sepsis. *Maximum temperature*—103.2°. *Leukocytes*—10,700; polynuclears, 77 per cent. *Blood culture*—*Streptococcus hemolyticus*; no growth in solid media. *Treatment*—Left salpingo-oöphorectomy; posterior colpotomy; drainage; vaccines. *Result*—Cured.

CASE No. 123, A. 1495.—*Age*—Twenty-seven years. *Diagnosis*—Scarlet fever; bacteriemia. *Maximum temperature*—105.3°. *Leukocytes*—15,000; polynuclears, 93 per cent. *Blood culture*—*Streptococcus hemolyticus*; four positive cultures within a period of four days, from 2 to 100 per c.c. *Treatment*—Partial mastoidectomy; phlebotomy of left lateral sinus. *Result*—Cured.

CASE No. 124, A. 198.—*Age*—Twenty-four years. *Diagnosis*—Acute otitis media; bacteriemia. *Maximum temperature*—101°. *Leukocytes*—14,900; polynuclears, 78.5 per cent. *Blood culture*—*Streptococcus hemolyticus*; 6 per c.c. *Treatment*—Paracentesis. *Result*—Cured.

CASE No. 125, A. 370.—*Age*—Thirty-two years. *Diagnosis*—Septic infarcts of kidney, sepsis. *Maximum temperature*—104.6°. *Leukocytes*—15,000; polynuclears, 83 per cent. *Blood culture*—*Streptococcus hemolyticus*, two positive cultures on following days; 5 per c.c. in second. *Treatment*—Palliative. *Result*—Cured.

CASE No. 126, A. 5223.—*Age*—Twenty years. *Diagnosis*—Abscess of breast; bacteriemia. *Maximum temperature*—106.3°. *Leukocytes*—32,000; polynuclears, 93 per cent. *Blood culture*—*Streptococcus hemolyticus*; 3.5 per c.c.; two negative cultures during the following six days. *Treatment*—Multiple incisions and drainage. *Results*—Cured.

## STREPTOCOCCUS HEMOLYTICUS—IMPROVED.

CASE No. 13, B. 2492.—*Age*—Twenty-one years. *Diagnosis*—Gunshot wound of chest; bacteriemia. *Maximum temperature*—105°. *Leukocytes*—26,000; polynuclears, 90 per cent. *Blood culture*—Streptococcus hemolyticus; two positive cultures within a period of a few days; no growth in solid media in either. *Treatment*—Tetanus antitoxin; vaccines. *Result*—Improved.

## STREPTOCOCCUS HEMOLYTICUS—UNIMPROVED.

CASE No. 41, D. 6225.—*Age*—Nineteen years. *Diagnosis*—Acute tonsillitis; sepsis. *Maximum temperature*—105.4°. *Leukocytes*—17,800; polynuclears, 97 per cent. *Blood culture*—Streptococcus hemolyticus, number of colonies not noted. *Treatment*—Palliative. *Result*—Unimproved.

CASE No. 54, C. 517.—*Age*—Twenty-two years. *Diagnosis*—Incomplete abortion; sepsis. *Maximum temperature*—103°. *Blood culture*—Streptococcus hemolyticus: 110 per c.c. *Treatment*—Palliative. *Result*—Unimproved.

## STREPTOCOCCUS HEMOLYTICUS—DIED.

CASE No. 5, A. 3785.—*Age*—Thirty years. *Diagnosis*—Cellulitis of forearm; bacteriemia. *Maximum temperature*—106.3°. *Blood culture*—Streptococcus hemolyticus: 2 per c.c. *Treatment*—Incision and drainage. *Result*—Died.

CASE No. 10, D. 4165.—*Age*—Twelve years. *Diagnosis*—Acute septic endocarditis. *Maximum temperature*—106.8°. *Leukocytes*—9600; polynuclears, 69 per cent. *Blood culture*—Streptococcus hemolyticus, 110 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 14, D. 1850.—*Age*—Eighteen years. *Diagnosis*—Pseudoleukemia; sepsis. *Maximum temperature*—103.8°. *Leukocytes*—1400; polynuclears, 71.6 per cent. *Blood culture*—Streptococcus hemolyticus; two positive cultures within an interval of a few days; no growth in solid media. *Treatment*—Salvarsan, intravenously. *Result*—Died.

CASE No. 11, B. 2573.—*Diagnosis*—Cancer of breast; infection of wound; sepsis. *Maximum temperature*—105.2°. *Leukocytes*—16,200; polynuclears, 87 per cent. *Blood culture*—Streptococcus hemolyticus; two positive cultures within a period of a few days: 1 per c.cm in first; few colonies of streptococcus in second, accompanied by Staphylococcus pyogenes aureus. *Treatment*—Complete mastectomy, with removal of pectoral muscles and axillary lymph glands. *Result*—Died.

CASE No. 12, C. 1476.—*Age*—Twenty-two years. *Diagnosis*—Ectopic gestation; rupture; bacteriemia. *Maximum temperature*—

100°. *Leukocytes*—16,400; polynuclears, 82 per cent. *Blood culture*—*Streptococcus hemolyticus*, innumerable colonies. *Treatment*—Partial hysterectomy. *Result*—Died.

CASE No. 16, D. 1358.—*Age*—Twenty months. *Diagnosis*—Otitis media; sepsis. *Maximum temperature*—107.6°. *Blood culture*—*Streptococcus hemolyticus*, 120 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 22, A. 335.—*Diagnosis*—Complete abortion; sepsis. *Maximum temperature*—104.6°. *Leukocytes*—27,400; polynuclears, 91 per cent. *Blood culture*—*Streptococcus hemolyticus*, colonies few, number not noted. *Treatment*—Vaccines. *Results*—Died.

CASE No. 23, B. 11.—*Age*—Nineteen years. *Diagnosis*—Acute salpingitis; peritonitis; pneumonia; sepsis. *Maximum temperature*—105.6°. *Leukocytes*—22,800; polynuclears, 87 per cent. *Blood culture*—*Streptococcus hemolyticus*, abundant growth; number of colonies not noted. *Treatment*—Palliative. *Result*—Died.

CASE No. 27, 1909, III, 8.—*Age*—Twenty-five years. *Diagnosis*—Puerperal sepsis. *Maximum temperature*—105.8°. *Leukocytes*—11,200; polynuclears, 88 per cent. *Blood culture*—*Streptococcus hemolyticus*; two positive cultures within a period of a few days: 8 per c.c. in first; number not noted in second. *Treatment*—Vaccines; serum. *Result*—Died.

CASE No. 32, C. 383.—*Age*—Thirty-two years. *Diagnosis*—Pelvic cellulitis; polyarthrits; sepsis. *Maximum temperature*—104.4°. *Leukocytes*—9400; polynuclears, 76 per cent. *Blood culture*—*Streptococcus hemolyticus*; three positive cultures within a period of three or four days, three to seven colonies per c.c. *Treatment*—Incision and drainage of abscess of knees. *Result*—Died.

CASE No. 33, C. 667.—*Age*—Eighteen years. *Diagnosis*—Post-partum sepsis. *Maximum temperature*—105°. *Leukocytes*—21,000; polynuclears, 86 per cent. *Blood culture*—*Streptococcus hemolyticus*: 12 per c.c. *Treatment*—Serum. *Result*—Died.

CASE No. 38, D. 4589.—*Age*—Thirty-one years. *Diagnosis*—Chronic + acute endocarditis; chronic nephritis; chronic pulmonary tuberculosis. *Maximum temperature*—106°. *Leukocytes*—35,100; polynuclears, 92 per cent. *Blood cultures*—*Streptococcus hemolyticus*: 110 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 46, D. 3825.—*Age*—Fifty-seven years. *Diagnosis*—Sepsis. *Maximum temperature*—106.6°. *Leukocytes*—4400; polynuclears, 85 per cent. *Blood culture*—*Streptococcus hemolyticus*: 100 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 47, D. 4914.—*Age*—Twenty-one years. *Diagnosis*—Acute lymphatic leukemia; sepsis. *Maximum temperature*—105.6°. *Leukocytes*—28,900; polynuclears, 1 per cent. *Blood culture*—*Streptococcus hemolyticus*; only fluid media used. *Treatment*—Palliative. *Result*—Died.

CASE No. 48, D. 4946.—*Diagnosis*—Sepsis. *Maximum temperature*—105°. *Leukocytes*—7,200; polynuclears, 92 per cent. *Blood culture*—*Streptococcus hemolyticus*; two positive cultures on following days, 360 per c.c. in latter. *Treatment*—Palliative. *Result*—Died.

CASE No. 50, C. 2918.—*Age*—Thirty-six years. *Diagnosis*—Complete abortion; sepsis. *Maximum temperature*—108°. *Leukocytes*—17,200; polynuclears, 93 per cent. *Blood culture*—*Streptococcus hemolyticus*, number of colonies not noted. *Treatment*—Palliative. *Result*—Died.

CASE No. 51, B. 5597, C. 4816.—*Age*—Thirty-four years. *Diagnosis*—Acute endometritis; thrombophlebitis of pelvic veins; sepsis; *Maximum temperature*—105.6°. *Leukocytes*—4400; polynuclears, 80 per cent. *Blood culture*—*Streptococcus hemolyticus*; four positive cultures within a period of two weeks, from 1 to 100 per c.c. *Treatment*—Serum; transfusion; pelvic drainage. *Result*—Died.

CASE No. 55, C. 2044.—*Age*—Twenty-two years. *Diagnosis*—Incomplete abortion; sepsis. *Maximum temperature*—106.2°. *Leukocytes*—12,000; polynuclears, 96 per cent. *Blood culture*—*Streptococcus hemolyticus*: 250 per c.c. *Treatment*—Vaccines. *Result*—Died.

CASE No. 89, D. 1116.—*Age*—Ten years. *Diagnosis*—Typhoid fever; streptococcus; bacteriemia. *Maximum temperature*—106.2°. *Leukocytes*—15,000; polynuclears, 88 per cent. *Blood culture*—*Bacillus typhosus* and *Streptococcus hemolyticus*; only fluid media used. *Treatment*—Typhoid; salicylates. *Result*—Died.

CASE No. 24, C. 114.—*Age*—Twenty-nine years. *Diagnosis*—Abscess of uterus; sepsis. *Maximum temperature*—101.6°. *Leukocytes*—67,000; polynuclears, 95 per cent. *Blood culture*—*Streptococcus hemolyticus*, number of colonies not noted. *Treatment*—Complete hysterectomy. *Result*—Died.

CASE No. 28, 1909, IX, 11.—*Age*—Thirty-eight years. *Diagnosis*—Sepsis. *Maximum temperature*—106.4°. *Leukocytes*—22,000; polynuclears, 84 per cent. *Blood culture*—*Streptococcus hemolyticus*; number of colonies not noted. *Treatment*—Curettage; bilateral trachelorrhaphy. *Result*—Died.

#### STREPTOCOCCUS MUCOSUS—DIED.

CASE No. 36, A. 2498.—*Age*—Fourteen years. *Diagnosis*—Fracture of base; suppurative meningitis; sepsis. *Maximum temperature*—106°. *Leukocytes*—19,000; polynuclears, 81 per cent. *Blood culture*—*Streptococcus mucosus*, 1 per c.c. *Treatment*—Vaccines. *Result*—Died.



## STAPHYLOCOCCUS AUREUS—CURED.

CASE No. 59.—*Diagnosis*—Osteomyelitis of tibia; bacteriemia. *Blood culture*—Staphylococcus aureus: 1 per c.c. *Treatment*—Vaccines, amputation. *Result*—Cured.

CASE No. 60.—*Age*—Fifty years. *Diagnosis*—Panophthalmitis; frontal sinusitis; bacteriemia. *Blood culture*—Staphylococcus aureus: 1 per c.c. two days after operation. *Treatment*—Operation. *Result*—Cured.

CASE No. 97, A. 1670.—*Age*—Twenty-five years. *Diagnosis*—Infected wound of nose; bacteriemia. *Maximum temperature*—102.8°. *Leukocytes*—16,600; polynuclears, 70 per cent. *Blood culture*—Staphylococcus aureus, no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 111, A. 1695.—*Age*—Sixteen years. *Diagnosis*—Streptococcus; abscess of deep cervical glands; staphylococcus; bacteriemia. *Maximum temperature*—103.4°. *Leukocytes*—9000; polynuclears, 72 per cent. *Blood culture*—Staphylococcus aureus; no growth in solid media. *Treatment*—Excision of lymph nodes on left side of neck. *Result*—Cured.

CASE No. 112, B. 3967.—*Age*—Forty-two years. *Diagnosis*—Cellulitis of leg; bacteriemia. *Maximum temperature*—106°. *Blood culture*—Staphylococcus aureus; no growth in solid media; culture negative the following day and again three weeks later. *Treatment*—Multiple incisions and drainage. *Result*—Cured.

CASE No. 113, B. 4517.—*Diagnosis*—Sepsis. *Maximum temperature*—102.3°. *Leukocytes*—11,000; polynuclears, 72 per cent. *Blood culture*—Staphylococcus aureus; two positive cultures within a period of two days; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 114, A. 5096.—*Age*—Nine years. *Diagnosis*—Osteomyelitis of left tibia and of right radius; suppurative arthritis of right knee; sepsis. *Maximum temperature*—103.8°. *Leukocytes*—22,600; polynuclears, 84 per cent. *Blood culture*—Staphylococcus aureus; no growth in solid media. *Treatment*—Amputation of leg, partial osteotomy of right radius, incision and drainage of right patella; vaccines. *Result*—Cured.

CASE No. 115, A. 4815.—*Age*—Eighteen years. *Diagnosis*—Chronic suppurative osteomyelitis of humerus; bacteriemia. *Maximum temperature*—104°. *Leukocytes*—25,000; polynuclears, 88 per cent. *Blood culture*—Staphylococcus aureus; no growth in solid media. *Treatment*—Incision of outer aspect of lower third of arm; sequestrum removed. *Result*—Cured.

CASE No. 116, A. 4763.—*Age*—Thirty-two years. *Diagnosis*—Chronic suppurative osteomyelitis of tibia; bacteriemia. *Maximum temperature*—102.4°. *Blood culture*—Staphylococcus aureus;

no growth in solid media. *Treatment*—Sequestrotomy; partial osteotomy of tibia. *Result*—Cured.

CASE No. 117, D. 2058, B. 1954.—*Age*—Thirty-three years. *Diagnosis*—Subphrenic abscess; multiple skin abscesses; sepsis. *Maximum temperature*—102.8°. *Leukocytes*—11,000; polynuclears, 72 per cent. *Blood culture*—*Staphylococcus aureus*: 1 per c.c., culture one week later negative. *Treatment*—Appendix removed; abscess drained. *Result*—Cured.

CASE No. 118, C. 2457.—*Age*—Fifty-five years. *Diagnosis*—Left hydrosalpinx; bacteriemia. *Maximum temperature*—101°. *Leukocytes*—13,000; polynuclears, 88 per cent. *Blood culture*—*Staphylococcus aureus*; no growth in solid media. *Treatment*—Left salpingo-oöphorectomy. *Result*—Cured.

CASE No. 119, C. 4413.—*Age*—Twenty-six years. *Diagnosis*—Peritoneal abscess (pelvic) bacteriemia. *Maximum temperature*—104°. *Leukocytes*—16,000; polynuclears, 90 per cent. *Blood cultures*—*Staphylococcus aureus*; no growth in solid media; there were two negative cultures, one preceding the other following the positive culture by one month. *Treatment*—Posterior colpotomy. *Result*—Cured.

CASE 121, A. 1812.—*Age*—Thirty-one years. *Diagnosis*—Chronic otitis; chronic mastoiditis; chronic appendicitis, bacteriemia. *Maximum temperature*—101°. *Leukocytes*—14,200; polynuclears, 81.5 per cent. *Blood cultures*—*Staphylococcus aureus*; no growth in solid media accompanied by *Streptococcus viridans*. *Treatment*—Appendectomy. *Result*—Cured.

CASE No. 122, D. 3407.—*Diagnosis*—Sepsis. *Maximum temperature*—105°. *Leukocytes*—15,400; polynuclears, 78 per cent. *Blood culture*—*Staphylococcus aureus*; three positive cultures within a period of twenty-five days: 1 per c.c. largest number of colonies. *Treatment*—Palliative. *Result*—Cured.

#### STAPHYLOCOCCUS AUREUS—IMPROVED.

CASE No. 77, A. 5775.—*Age*—Twelve years. *Diagnosis*—Osteomyelitis of humerus; bacteriemia. *Maximum temperature*—104°. *Leukocytes*—18,000; polynuclears, 84 per cent. *Blood culture*—*Staphylococcus aureus*; three positive cultures within a period of a week; no growth in solid media. *Treatment*—Osteotomy, vaccines. *Result*—Improved.

CASE No. 80, D. 3975.—*Age*—Fifteen years. *Diagnosis*—Chronic endocarditis; sepsis. *Maximum temperature*—102°. *Leukocytes*—11,400; polynuclears, 79 per cent. *Blood culture*—*Staphylococcus aureus*; no growth in solid media; culture four days later negative. *Treatment*—Salicylates. *Result*—Improved.

CASE No. 133, A. 1911.—*Age*—Fifty years. *Diagnosis*—Prostatic hypertrophy; sepsis. *Maximum temperature*—104°. *Leuko-*

*cytes*—12,000; polynuclears, 77 per cent. *Blood culture*—*Staphylococcus aureus*, number of colonies not noted; probably an instance of bacteriemia of urethral chill. *Treatment*—Prostatectomy. *Result*—Improved.

STAPHYLOCOCCUS AUREUS—DIED.

CASE No. 11, B. 2573.—*Diagnosis*—Cancer of breast; infection of wound; sepsis. *Maximum temperature*—105.2°. *Leukocytes*—16,200; polynuclears, 87 per cent. *Blood culture*—*Staphylococcus aureus*, accompanied by a few colonies of *Streptococcus hemolyticus*. *Treatment*—Complete mastectomy, with removal of pectoral muscles and axillary lymph glands. *Result*—Died.

CASE No. 31, 1909, XII, 11.—*Age*—Fourteen years. *Diagnosis*—Acute epiphysitis of hip; bacteriemia. *Maximum temperature*—106.2°. *Leukocytes*—14,000; polynuclears, 80.5 per cent. *Blood culture*—*Staphylococcus aureus*; two positive cultures within a period of several days; number of colonies not noted. *Treatment*—Incision and drainage of abscess about hip; vaccines. *Result*—Died.

CASE No. 56, B. 3814.—*Age*—Sixteen years. *Diagnosis*—Osteomyelitis; suppurative arthritis; sepsis. *Maximum temperature*—104.2°. *Leukocytes*—30,000; polynuclears, 88 per cent. *Blood culture*—*Staphylococcus aureus*, two positive cultures within a period of several weeks; 3 per c.c. in first, 1 per c.c. in second. *Treatment*—Incision of knee. *Result*—Died.

CASE No. 57, A. 3683.—*Age*—Eleven years. *Diagnosis*—Multiple abscesses; sepsis. *Maximum temperature*—104°. *Leukocytes*—37,200; polynuclears, 87 per cent. *Blood culture*—*Staphylococcus aureus*; no growth in solid media. *Treatment*—Incision and drainage of abscess of thigh. *Result*—Died.

CASE No. 62, D. 6438, A. 5346.—*Age*—Thirty-nine years. *Diagnosis*—Lumbar abscess; sepsis. *Maximum temperature*—105.6°. *Leukocytes*—16,000; polynuclears, 86 per cent. *Blood culture*—*Staphylococcus aureus*; two positive cultures within a period of a few days: 9 per c.c. in first, numerous in second. *Treatment*—Exploration of lumbar region. *Result*—Died.

CASE No. 63, E. 317, B. 5317, B. 5336.—*Age*—Two years, eight months. *Diagnosis*—Osteomyelitis of rib; sepsis. *Maximum temperature*—105°. *Leukocytes*—24,000; polynuclears, 91 per cent. *Blood culture*—*Staphylococcus aureus*: many per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 64, D. 4707.—*Age*—Thirty-nine years. *Diagnosis*—Pulmonary tuberculosis; sepsis. *Maximum temperature*—105.8°. *Leukocytes*—19,900; polynuclears, 86 per cent. *Blood culture*—*Staphylococcus aureus*: 300 per c.c.; culture about six weeks, later negative. *Treatment*—Palliative. *Result*—Died.

CASE No. 65, 1909, VII, 30. — *Age*—Thirty-eight years. *Diagnosis*—Chronic endocarditis. *Maximum temperature*—104.6°. *Leukocytes*—17,500; polynuclears, 86 per cent. *Blood culture*—*Staphylococcus aureus*: 1 per c.c.; culture few days earlier negative. *Treatment*—Palliative. *Result*—Died.

CASE No. 66, D. 6258. — *Age*—Thirty-eight years. *Diagnosis*—Phlebitis of portal vein; pericarditis; chronic endocarditis; sepsis. *Maximum temperature*—107°. *Leukocytes*—10,000; polynuclears, 91 per cent. *Blood culture*—*Staphylococcus aureus*; several colonies per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 76, B. 4336. — *Age*—Twenty-nine years. *Diagnosis*—Cholelithiasis; chronic appendicitis; sepsis. *Maximum temperature*—107°. *Blood culture*—*Staphylococcus aureus* + *Bacillus coli*; no growth in solid media. *Treatment*—Cholecystectomy; appendectomy. *Result*—Died.

CASE No. 78. — *Age*—Thirty years. *Diagnosis*—Typhoid fever; sepsis. *Blood culture*—*Staphylococcus aureus*; no growth in solid media. *Treatment*—Typhoid. *Result*—Died.

CASE No. 79, D. 3214. — *Age*—Forty-seven years. *Diagnosis*—Chronic endocarditis; sepsis. *Maximum temperature*—105°. *Leukocytes*—15,000; polynuclears, 89 per cent. *Blood culture*—*Staphylococcus aureus*; two positive cultures on following days: in each innumerable colonies. *Treatment*—Palliative. *Report*—Died.

CASE No. 81, B. 3479. — *Age*—Fifteen years. *Diagnosis*—Osteomyelitis; sepsis. *Maximum temperature*—105.6°. *Leukocytes*—13,600; polynuclears, 87 per cent. *Blood culture*—*Staphylococcus aureus*, two positive cultures on following days: 100 per c.c. in first, 15 per c.c. in second. *Treatment*—Incision and drainage of cellulitis of thigh; vaccines. *Result*—Died.

CASE No. 82, D. 4356. — *Age*—Thirty-nine years. *Diagnosis*—Meningitis; sepsis. *Maximum temperature*—106.6°. *Leukocytes*—50,000; polynuclears, 65.8 per cent. *Blood culture*—*Staphylococcus aureus*: 60 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 83, A. 4039. — *Age*—Seventeen years. *Diagnosis*—Osteomyelitis; arthritis; sepsis. *Maximum temperature*—106.4°. *Leukocytes*—18,000; polynuclears, 89 per cent. *Blood culture*—*Staphylococcus aureus*; three positive cultures within a period of a few days: 10 per c.c. in last one. *Treatment*—Partial ostectomy of tibia with drainage; arthrotomy with drainage. *Result*—Died.

CASE No. 84. — *Age*—Fifty years. *Diagnosis*—Femoral phlebitis; colitis; sepsis. *Maximum temperature*—101°. *Blood culture*—*Staphylococcus aureus*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 85, B. 4564. — *Diagnosis*—Septic infarct of kidney; acute nephritis; sepsis. *Maximum temperature*—102.4°. *Leukocytes*—18,000; polynuclears, 89 per cent. *Blood culture*—*Staphylococcus aureus*; abundant growth; number not noted. *Treatment*—Palliative. *Result*—Died.

CASE No. 93, 1909, VI, 7.—*Age*—Forty-eight years. *Diagnosis*—Sepsis. *Maximum temperature*— $107.8^{\circ}$ . *Leukocytes*—33,000; polynuclears, 85.5 per cent. *Blood culture*—*Staphylococcus aureus*; abundant growth; number not noted; *Staphylococcus aureus* from abscess of back. *Treatment*—Palliative. *Result*—Died.

CASE No. 94, 1909, XII, 11.—*Age*—Fourteen years. *Diagnosis*—Acute epiphysitis of hip; sepsis. *Maximum temperature*— $106.2^{\circ}$ . *Leukocytes*—14,000; polynuclears, 80.5 per cent. *Blood culture*—*Staphylococcus aureus*: 12 per c.c. *Treatment*—Incision and drainage of abscess about hip; vaccines. *Result*—Died.

CASE No. 95, D. 163.—*Age*—Twenty years. *Diagnosis*—Sepsis. *Maximum temperature*— $107.8^{\circ}$ . *Leukocytes*—42,000; polynuclears, 85 per cent. *Blood culture*—*Staphylococcus aureus*; abundant growth; number not noted. *Treatment*—Palliative. *Result*—Died.

CASE No. 96, B. 763.—*Age*—Twenty-six years. *Diagnosis*—Cellulitis of foot; pleurisy; sepsis. *Maximum temperature*— $107.4^{\circ}$ . *Leukocytes*—21,600; polynuclears, 89 per cent. *Blood culture*—*Staphylococcus aureus*; abundant growth; number not noted. *Treatment*—Incision; palliative. *Result*—Died.

CASE No. 86.—*Diagnosis*—Chronic endocarditis; acute prostatitis; infarct of kidney; sepsis. *Maximum temperature*— $103^{\circ}$ . *Blood culture*—*Staphylococcus aureus*: 30 per c.c. *Result*—Died.

#### STAPHYLOCOCCUS ALBUS—CURED.

CASE No. 120, D. 1030.—*Age*—Forty-eight years. *Diagnosis*—Typhoid fever; acute orchitis and epididymitis; bacteriemia. *Maximum temperature*— $105.6^{\circ}$ . *Leukocytes*—5,700; polynuclears, 51 per cent. *Blood culture*—*Staphylococcus albus*; abundant growth; number not noted. *Treatment*—Palliative. *Result*—Cured.

#### STAPHYLOCOCCUS ALBUS—DIED.

CASE No. 58, D. 1812.—*Age*—Thirty-six years. *Diagnosis*—Chronic and acute endocarditis. *Maximum temperature*— $103.6^{\circ}$ . *Leukocytes*—35,600. *Blood culture*—*Staphylococcus albus*; four positive cultures within a period of a few days; no growth in solid media; *Bacillus influenzae* accompanied *Staphylococcus albus* in each instance. *Treatment*—Palliative. *Result*—Died.

CASE No. 92, 1909, V, 7.—*Age*—Fifty. *Diagnosis*—Septic endocarditis. *Maximum temperature*— $104.8^{\circ}$ . *Leukocytes*—10,000; polynuclears, 78 per cent. *Blood culture*—*Staphylococcus albus*; three positive cultures within a period of two or three weeks: 5 per c.c. largest number of colonies. *Treatment*—Vaccines. *Result*—Died.

## PNEUMOCOCCUS—CURED.

CASE No. 103, D. 5360.—*Age*—Thirty-eight years. *Diagnosis*—Typhoid fever; lobar pneumonia. *Maximum temperature*—105.2°. *Leukocytes*—8600; polynuclears, 66 per cent. *Blood culture*—Pneumococcus; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

CASE No. 107, D. 6041.—*Age*—Forty-seven years. *Diagnosis*—Suppurative pericarditis; lobar pneumonia; suppurative pleurisy; arthritis of right wrist; sepsis. *Maximum temperature*—103.2°. *Leukocytes*—63,200; polynuclears, 98 per cent. *Blood culture*—Pneumococcus; no growth in solid media; culture a few days later negative. *Treatment*—Serum intravenously; incision and drainage of pericardium and pleura. *Result*—Cured.

## PNEUMOCOCCUS—UNIMPROVED.

CASE No. 3, D. 4909.—*Age*—Thirty-one years. *Diagnosis*—Sepsis. *Maximum temperature*—105.4°. *Leukocytes*—9,800; polynuclears, 77 per cent. *Blood culture*—Pneumococcus; two positive cultures within a period of a few days. *Treatment*—Palliative. *Result*—Unimproved.

CASE No. 8, D. 4142.—*Age*—Four years. *Diagnosis*—Bronchopneumonia; otitis media. *Maximum temperature*—106°. *Leukocytes*—14,000; polynuclears, 77 per cent. *Blood culture*—Pneumococcus; colonies few; number not noted. *Treatment*—Incision of ear drum. *Result*—Unimproved.

## PNEUMOCOCCUS—DIED.

CASE No. 34, D. 1689.—*Age*—Eight years. *Diagnosis*—Chronic and acute endocarditis; meningitis. *Maximum temperature*—108°. *Leukocytes*—21,000; polynuclears, 89 per cent. *Blood culture*—Pneumococcus; colonies abundant; number not noted. *Treatment*—Salicylates. *Result*—Died.

CASE No. 35, D. 1780.—*Age*—Thirty-eight years. *Diagnosis*—Chronic otitis media; sepsis. *Maximum temperature*—106.2°. *Leukocytes*—28,300; polynuclears, 94 per cent. *Blood culture*—Pneumococcus: 2 per c.c. *Treatment*—Palliative. *Result*—Died.

CASE No. 100, B. 2339.—*Age*—Forty-eight years. *Diagnosis*—Acute appendicitis; peritoneal abscess; sepsis. *Maximum temperature*—106°. *Leukocytes*—9800; polynuclears, 79 per cent. *Blood culture*—Pneumococcus: 4 per c.c. *Treatment*—Appendectomy with drainage; transpleural hepatotomy. *Result*—Died.

CASE No. 101, A. 3767.—*Age*—Thirty-two years. *Diagnosis*—Abscess of brain; sepsis. *Maximum temperature*—105.8°. *Leukocytes*—18,000; polynuclears, 90 per cent. *Blood culture*—Pneumo-

coccus; innumerable colonies. *Treatment*—Palliative. *Result*—Died.

CASE No. 104, E. 251.—*Age*—Three months. *Diagnosis*—Pneumococcus meningitis. *Maximum temperature*—105.4°. *Leukocytes*—17,000; polynuclears, 77 per cent. *Blood culture*—Pneumococcus; innumerable colonies. *Treatment*—Serum. *Result*—Died.

CASE No. 72, B. 1197.—*Age*—Sixty-two years.—*Diagnosis*—Sepsis; empyema. *Maximum temperature*—104.2° *Leukocytes*—64,000; polynuclears, 92 per cent. *Blood culture*—Pneumococcus; no growth in solid media. *Treatment*—Thoracotomy. *Result*—Died.

#### BACILLUS COLI—CURED.

CASE No. 75, A. 3142.—*Age*—Twenty-eight years. *Diagnosis*—Mastoiditis; bacteriemia. *Maximum temperature*—106°. *Leukocytes*—15,000; polynuclears, 81 per cent. *Blood culture*—Bacillus coli; 1 per c.c. *Treatment*—Partial mastoidectomy. *Result*—Cured.

CASE No. 87, D. 957.—*Age*—Thirty-four years. *Diagnosis*—Gastro-enteritis; bacteriemia. *Maximum temperature*—102.4°. *Leukocytes*—7800; polynuclears, 60 per cent. *Blood culture*—Bacillus coli; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

#### BACILLUS COLI—DIED.

CASE No. 37, C. 2292.—*Age*—Twenty-nine years. *Diagnosis*—Acute diffuse peritonitis; pelvic cellulitis; meningitis; sepsis. *Maximum temperature*—106.6°. *Leukocytes*—19,500; polynuclears, 89 per cent. *Blood culture*—Bacillus coli; few with Streptococcus viridans. *Treatment*—Palliative. *Result*—Died.

CASE No. 90, D. 3427, D. 2037.—*Age*—Three years. *Diagnosis*—Raynaud's disease; bacteriemia. *Maximum temperature*—105.2°. *Leukocytes*—26,400; polynuclears, 71 per cent. *Blood culture*—Bacillus coli, only fluid media used. *Treatment*—Amputation of right arm, two fingers, and right leg. *Result*—Died.

CASE No. 98, C. 2200.—*Age*—Fifty-three years. *Diagnosis*—Carcinoma of cervix; sepsis, postoperative. *Maximum temperature*—103.8°. *Leukocytes*—8800; polynuclears, 77 per cent. *Blood culture*—Bacillus coli; two positive cultures: 15 per c.c.; Bacillus coli in first, Bacillus coli and Bacillus proteus the following day; no growth in solid media. *Treatment*—Complete hysterectomy. *Result*—Died.

CASE No. 76, B. 4336.—*Age*—Twenty-nine years. *Diagnosis*—Cholelithiasis; chronic appendicitis; sepsis. *Maximum temperature*—107°. *Blood culture*—Bacillus coli and aureus; no growth in solid media. *Treatment*—Cholecystectomy, appendectomy. *Result*—Died.

## BACILLUS INFLUENZÆ—DIED.

CASE No. 58, D. 1812.—*Age*—Thirty-six years. *Diagnosis*—Chronic + acute endocarditis. *Maximum temperature*—103.6°. *Leukocytes*—35,600 per cent. *Blood culture*—*Bacillus influenzae*; four positive cultures within a period of a few days; no growth in solid media; *Staphylococcus albus* accompanied *Bacillus influenzae* in each instance. *Treatment*—Palliative. *Result*—Died.

CASE No. 67.—*Age*—Thirty years. *Diagnosis*—Subacute endocarditis. *Blood culture*—*Bacillus influenzae*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

## ANAEROBIC STREPTOCOCCI—CURED.

CASE No. 131, C. 2238.—*Age*—Thirty-two years. *Diagnosis*—Pyosalpinx; pelvic abscess; thrombophlebitis of left femoral; bacteriemia. *Maximum temperature*—105.2°. *Leukocytes*—28,400; polynuclears, 89 per cent. *Blood culture*—Anaerobic streptococci; no growth in solid media. *Treatment*—Posterior colpotomy with drainage. *Result*—Cured.

## ANAEROBIC STREPTOCOCCI—DIED.

CASE No. 52, D. 3900.—*Age*—Thirty years. *Diagnosis*—Acute endometritis; sepsis. *Maximum temperature*—104.6°. *Leukocytes*—10,600; polynuclears, 70 per cent. *Blood culture*—Anaerobic streptococci; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 53, C. 1915.—*Age*—Forty years. *Diagnosis*—Pyosalpinx; sepsis. *Maximum temperature*—102.6°. *Leukocytes*—25,400; polynuclears, 86 per cent. *Blood culture*—Anaerobic streptococci; no growth in solid media; an anaerobic streptococcus and *Bacillus coli* obtained from culture of pus from left uterine tube. *Treatment*—Complete abdominal hysterectomy; right and left salpingo-oophorectomy; appendectomy; division of adhesions; enterorrhaphy. *Result*—Died.

## BACILLUS MUCOSUS CAPSULATUS—CURED.

CASE No. 108, D. 6526.—*Age*—Forty-five years. *Diagnosis*—Sepsis. *Maximum temperature*—106.3°. *Leukocytes*—13,800; polynuclears, 90 per cent. *Blood culture*—*Bacillus mucosus capsulatus*; three positive cultures within a period of four days; growth in fluid media in all; in one only a growth in solid media of 3 or 4 colonies per c.c. Three negative cultures during the following six weeks. *Treatment*—Fixation abscess; incision and drainage of right leg. *Result*—Cured.



# BACILLUS MALLEI—DIED.

CASE No. 99, D. 1140.—*Age*—Thirty-eight years. *Diagnosis*—Glanders. *Maximum temperature*—105.6°. *Blood culture*—*Bacillus mallei*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

CASE No. 132, D. 1737.—*Age*—Thirty-seven years. *Diagnosis*—Glanders, balanoposthitis. *Maximum temperature*—105.4°. *Leukocytes*—26,000; polynuclears, 87 per cent. *Blood culture*—*Bacillus mallei*; no growth in solid media. *Treatment*—Palliative. *Result*—Died.

# BACILLUS FECALIS ALKALIGENES—CURED.

CASE No. 134.—*Age*—Thirty years. *Diagnosis*—Gastroenteritis. *Blood culture*—*Bacillus fecalis alkaligenes*; no growth in solid media. *Treatment*—Palliative. *Result*—Cured.

## DIABETES IN CHINA.

By ALFRED C. REED, M.D.,

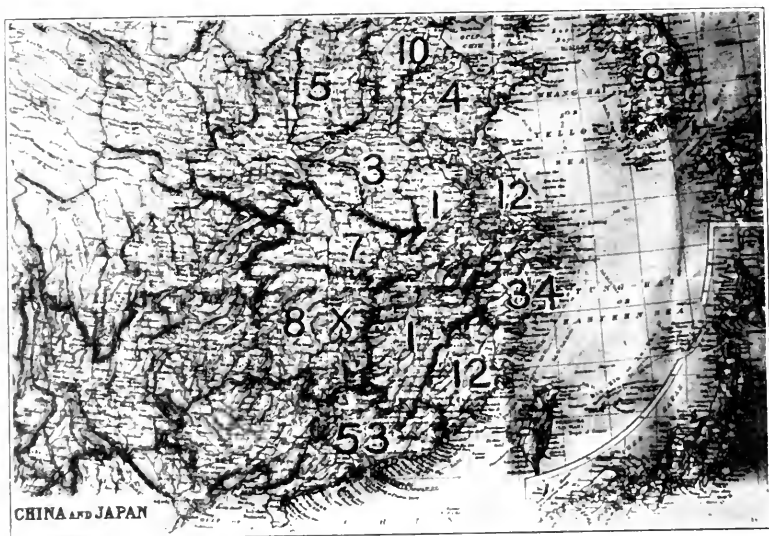
YALE HOSPITAL, CHANGSHA, CHINA.

It has long been accepted that diabetes mellitus does not occur in the tropics and the Orient, or at least that its occurrence there is infrequent. Not much definite information is available on this point. That the situation, however, is either changing or better understood is indicated by an item in the India correspondence of the *British Medical Journal*, October 3, 1914 (p. 604), to the effect that the Madras Government, being impressed by the serious frequency of diabetes among the educated classes of that presidency, has appointed an investigator who is to give three years' study to the problems of causation and prevention. In regard to China, opinion is vague as to the prevalence of diabetes and the reasons for it.

To secure the data here presented, a questionnaire was sent to 150 representative western physicians scattered as evenly as possible through the eighteen provinces of China and Korea. Sixty-three replies were received, of which 28 reported no cases observed in periods of from eighteen months to thirty years' medical experience in China. Of the remaining 35 a number of case reports were so inexact and the diagnosis so lacking in adequate support as to preclude their consideration. Apparently reliable reports were obtained of 206 cases of diabetes mellitus,<sup>1</sup> of which the great

<sup>1</sup> Since preparing the above report, one case of diabetes mellitus has been treated in the Yale Hospital, making the total list 207 cases. This case died after two days in coma.

majority had been observed within the last five years. There were distributed by provinces as follows: Kwantung 53, Chekiang 34, Kiangsu 12, Fukien 12, Chihli 10, Hunan 8, Korea 8, Hupei 7, Formosa 6, Shansi 5, Shantung 4, Honan 3, Anhwei and Kiangsi 1 each; 42 not stated. Thus positive reports are in hand from 12 of the 18 provinces of China proper, as also from Korea and Formosa. The 28 negative reports were distributed by provinces as follows: 3 each from Korea, Chihli, Hupei, Hunan, Anhwei, and Manchuria; 2 each from Kwantung, Kiangsu and Szechuen; 1 from Honan and 3 not stated. No reports were received from Kwangsi, Yunnan, Kweichow, Shensi, and Kansu. There was a great diversity of opinion as to the relative incidence within China, observers in north or central China believing the disease more prevalent in southern and eastern districts, and *vice versa*.



Map showing distribution of diabetic cases by provinces.

Of the 164 cases which can be placed geographically, the largest number are in the coast provinces of Kwantung, Fukien, Chekiang and Kiangsu. These figures may not indicate a greater incidence in this area, but exact comparisons are nearly impossible to give. Various more or less indeterminate factors must be considered, such as the average temperament, social status and predisposition of the patients, the presence or absence of routine urine examinations, and the care and skill of the doctor in eliminating non-diabetic glycosuria. Until more exhaustive data are available, covering the entire 18 provinces, the question of relative incidence must be left in abeyance. Speculation from insufficient data is futile.

In none of the reported cases was definite hereditary predisposition noted. Of 136 cases where the sex was stated, 118 were in

males and 18 in females. This is not significant, as the great majority of all patients are males. So, too, with the age. Exactly two-thirds were between thirty and fifty years of age, but the majority of patients coming to hospitals and clinics are probably between these limits.

Age.	Cases.	Per cent.
Under 20 . . . . .	4	2.9
21 to 30 . . . . .	32	23.2
31 to 40 . . . . .	45	32.6
41 to 50 . . . . .	47	34.0
51 to 60 . . . . .	6	4.4
Over 61 . . . . .	4	2.9
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138		

Of 86 cases in which the occupation was stated, 48, or 55 per cent. were shopkeepers, tradesmen, or otherwise engaged in business; 20, or 23 per cent., were farmers. There were 8 housewives, 2 clerks, 1 tanner, 1 teacher, 1 coolie, 1 peddler, 1 soldier, and 3 men of means without occupation. In 26 cases the complaints for which medical relief was sought were noted as follows: 10 emaciation, 9 debility, 15 excessive thirst, 12 polyuria, 12 headache, 2 loss of weight, 4 pruritus, 3 peripheral nervous symptoms, 1 furunculosis, and 1 chronic cough. Closer examination of 64 cases showed a large percentage to be suffering from cataract and multiple abscesses. Dyspepsia, dysentery, and carbuncle were noted in three cases each, and pyemia, erysipelas, bronchopneumonia, and cryptogenic splenomegaly were found in one each. It is to be regretted that fuller information could not be elicited under these headings. It appears that patients presenting themselves with emaciation, polyuria, thirst, or headache, alone or in combination, especially if they have also multiple abscesses or cataract, and if no evident cause is found, should be examined for diabetes.

In 188 cases the predominant article of diet was named. In 130 rice was the staple and in 57 wheat, some of the latter adding millet, corn, beans, and sweet potatoes. Thus for the great majority, rice formed the main article of diet. It is out of the scope of this paper to do more than present the data collected. Fuller discussion is postponed to a later date.

Of 43 physicians who answered the question of relative prevalence, one considered diabetes more prevalent than in the west, 7 of equal frequency, and 35 considered it much less frequent. Among the reasons given for decreased frequency were the assumed fact that the Chinese as a race are hardier than western peoples, and that they resist nervous shocks better and have fewer of them. Little excitement and simple diet are adduced. One physician lays the decreased prevalence to the fact that the plain diet of rice and well-cooked vegetables with practically no sugars, is digested and absorbed so slowly as to prevent hyperglycemia. The

same correspondent continued that "the temperance habit (of the Chinese) in food and drink does not disturb the carbohydrate metabolism." It is at least an open question as to whether the Chinese as a race are as temperate in food and drink as this writer assumes. Fast eating without proper mastication, and periods of hunger terminated by most liberal and prodigious stuffing, together with a fairly constant consumption of alcohol, though rarely to the point of intoxication, are more characteristic of the race than is ordinarily supposed. It is more than possible that these factors may have a definite influence on the prevalence of arteriosclerosis and cardiac lesions, even in the first two decades of life. It is worth considering that the excessive lack of sugars in the average Chinese dietary, even in the presence of a maximum starch fraction, may well determine an increased tolerance for carbohydrates.

It is pointed out in a number of reports that diabetes in the Chinese is more prevalent in the better classes. This is probably true, and is confirmed by the distribution of the small series here reported, when it is remembered that the great bulk of the patients seen are from the lower classes. Dr. Lambert, of Kiukiang, whose observation and experience lend weight to his word, says: "I believe it has not until recently been a disease from which the Chinese have suffered much, but of late years, with the increased desire for foreign medical treatment evinced by Chinese of all classes, diabetes mellitus has been found to occur to quite an appreciable extent among the better classes." Lambert reported two cases of diabetes in the *British Medical Journal*, January 4, 1908, which were observed in Formosa. He also noted three cases of glycosuria in a series of 200 insurance examinations and one case of diabetes in 24,000 out-patients in Nanking, all drawn from the lower classes of society. He says, with reason: "Perhaps the idea that diabetes was an unknown disease among the Chinese arose from the fact that until comparatively recently foreign medical treatment was better appreciated by the coolie class than by the wealthier and more conservative merchants and officials, and because examination of wealthy natives for insurance was not so common in China ten years ago as it is today."

Dr. J. L. Maxwell, who found but two cases in 12,000 in-patients under accurate observation, concludes that he has no idea of the reason for decreased prevalence unless it be the absence of the hustle of the West. Even that he doubts, as he finds hysteria fairly common and both functional and organic nervous diseases not rare. Our experience at Changsha entirely confirms this statement. Dr. Maxwell, together with many, suggests the possible influence of racial tendencies and characteristics. It is useless at present to turn aside into this field, however attractive it appear, because it is as yet a field of speculation only. The peculiar racial psychology of the Chinese, based on controlled experimental data, is yet to be written.

Dr. Peill, of Tsangchow, Chihli, proposes the interesting thesis that "the only reason that occurs to me (for a prevalence less than in England) is the opposite of an unknown, *i. e.*, the opposite of that which makes it frequent among the Jews." Dr. J. P. Maxwell, who reports 11 cases from Yungchun, Fukien, considers diabetes more frequent than supposed. Dr. Park, from Soochow, Kiangsu, reports 8 cases in five years out of 3000 to 5000 persons seen annually. His practice is restricted to first-class patients. He says: "I used to think it infrequent, but the longer I stay in China the less am I inclined to make positive statements." This perhaps illustrates the probability already noted, that the rarity of diabetes in earlier and in many present reports may be in part explained by the fact that the great majority of patients coming to western hospitals are of the lower classes, where this disease is less apt to occur in any race.

Dr. Van Buskirk says that the disease is known to the Koreans, who call it the "sweet urine disease." He considers it rare, however. Another physician of thirty years' practice in Seoul had seen no case. Dr. Lewis, of Chenchow, Hunan, makes a comment which must always be borne in mind in a consideration of the prevalence of diabetes in China. He believes that the etiological factors ordinarily designated might be found as striking in China as in any prevalent district. Nevertheless, he considers diabetes very infrequent in south Hunan.

In regard to treatment, the prevailing opinion is that dietetic control with sufficient elimination of carbohydrates, brings the same results as in the West, but that dietetic control is usually impossible where rice forms the chief article of diet. Several favorable reports were received on the good results from substituting native oatmeal for rice. One diabetic dietary consisted of bran, meat, and goat's milk. One report described a case in a giant beggar, seven feet in height, who died in hospital. He was feeble-minded, and made his living by exhibiting his ability to eat five catties or seven pounds of bread at one sitting.

In view of the opinions at hand, representing the observation and experience of a large body of competent observers, the following conclusions seem justified:

1. In the predominant class of persons under medical observation in China, diabetes mellitus is less common than in the west.
2. It will, however, be found increasingly prevalent in China, as observation is extended more widely to the better classes of society.
3. The course of the disease and its response to treatment are parallel to similar conditions in the west.
4. No evidence is at hand indicating etiological factors different from those in the west. Theories accounting for a decreased prevalence may conceivably be refuted by widespread introduction of closer clinical examination.

## REVIEWS

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A TREATISE ON THE PRINCIPLES AND PRACTICE OF MEDICINE.  
By ARTHUR R. EDWARDS, A.M., M.D., Professor of the Principles and Practice of Medicine and Clinical Medicine and Dean of the Faculty in the Northwestern University Medical School, Chicago; Attending Physician to Michael Reese Hospital. Third edition. Pp. 1022; 80 engravings and 23 plates. Philadelphia and New York: Lea & Febiger, 1916.

THE recent advances in medicine is an aphorism oft repeated; the phrase is, however, a true one and is well exemplified in the present edition of Edward's treatise. Since the presentation of the last edition of the work many advances have been made in medicine, and most of those relating to internal medicine have been incorporated by the author in his text. For example, he has found it necessary to write practically new sections on ictero-anemia, the ductless glands, roentgen-ray findings, erythemia, sepsis, sporotrichosis, blastomy, trichinosis, hook-worm disease, pellagra, the cardiac arrhythmias, the numerous tropical diseases, anaphylaxis and a host of other disorders. The improvements in therapeutics are represented by the addition of Flexner's serum, tuberculin, the various forms of serum therapy, vaccines, salvarsan, as well as many less well-known drugs. In the present revision particularly praiseworthy are the amplifications in the chapters on tuberculosis and syphilis and the thorough discussion of such subjects as hypertension, constipation, drug addictions, and the neuralgias.

In the handling of each subject the general rule is followed to deal with under separate headings, the definition of the etiology, the symptoms, the diagnosis, the course and prognosis, and the treatment of the disease. This main plan is adhered to in all the disorders of more than minor importance while in the really important ones, or at least in the frequently seen diseases, there are separate headings devoted to the history, the pathology, the bacteriology, the differentiation, and the complications of the disease under discussion. In this way the author considers all the important phases of a disease, and yet is able to so condense the work that it makes a volume of good readable size which contains all the essentials in every particular.

The book can be highly praised, yet in several respects it would seem that certain criticisms might be made. The section on diseases

of the kidney seems to be one that is particularly deficient. The old pathological classification of renal disease is followed and no mention is made of the many functional tests that have been elaborated in the study of the nephropathies and upon which rational treatment depends. The discussion of the cardiac arrhythmias might well be enlarged, moreover, minor errors have crept into this section, as, for example, considering auricular flutter as synonymous with auricular fibrillation. The section devoted to gastric neuroses, a subject which one might say is a universal complaint, is extremely brief, while to typhoid fever, a rapidly decreasing disease, more space is allotted than to any other disease excepting tuberculosis.

These criticisms are more a question of opinion than a question of fact. With only an occasional error in facts here and there, the book is remarkably complete. It contains all the essentials; it is written in a lucid, clean-cut style, and it can be recommended as a most admirable text-book for the student or a reference book for the practitioner.

J. H. M., JR.

DISEASES OF THE ARTERIES, INCLUDING ANGINA PECTORIS. By SIR CLIFFORD ALLBUTT, K.C.B., Regius Professor of Physics in the University of Cambridge. In two volumes. Pp. 534 and 559. London: Macmillan & Co., 1915.

THERE are certain medical treatises which stand out, for one reason or another, books which will always be of value and will have to be consulted and referred to in any discussion of the subject with which they deal. This work takes a place among these, and is also to be welcomed as the *magnum opus* of one who has long held a prominent place in medicine. It is not easy to write with a proper view of the wide problems of a subject when one is full of the knowledge of the details, and arterial disease has far-reaching effects. In this work there are both breadth of vision and attention to detail.

The author has written a preface which should not be missed: it is delightful reading. There will be no one to disagree with him that the labor put into these volumes is honest labor. To his hope "that the winter fruitage of an old tree, if a little withered, may not be unsound," we may say (altering the quotation slightly) that "age cannot wither, nor custom state, your infinite variety." Professor Allbutt has dealt with many subjects and has never failed to throw light on any one which he has discussed.

*Diseases of the Arteries.* The discussion of this occupies one volume and part of the other. As introductory to the subject proper there are chapters on the physics of the circulation and the viscosity of the blood. It is not difficult for the majority of us to

be beyond our depth before we know it when we venture in these waters. The chapter on the causes of arteriosclerosis extends to over 150 pages, and every possible factor is fully considered. The influence of mechanical and many toxic causes are discussed. Concerning the importance of alcohol in the etiology it is regarded as not a very important cause in itself, but a potent ally of any other poison. Of any influence of tobacco the conclusion is that we have little definite proof. The author insists on the distinction between arterial lesions with high pressure and without it, one which he has emphasized for many years. Special attention is paid to a form which the author terms senile or "decreascent arteriosclerosis." This he considers may be a family form in which the arteries are especially susceptible to toxic influences. It is not necessarily associated with high pressure.

Special interest belongs to the discussion of "hyperpiesis," a term which the author introduced to describe the cases in which high blood-pressure exists without renal disease. There is much difference of opinion as to the existence of such a condition and many deny that it occurs. But the evidence seems to support Professor Allbutt's contention, and we must agree that there are causes other than renal for persistent hypertension. In certain of these cases the increased blood-pressure is the cause and not the result of arteriosclerosis. The author insists on the importance of this, particularly with reference to treatment. In his opinion, if recognized early, the condition may be entirely recovered from, and in the majority of cases materially aided. Many disagree with this, but it is undoubtedly worthy of consideration, and those opposed to it should read this discussion of it with an open mind. Growing out of this view is the author's belief that cerebral hemorrhage is more often the result of high pressure than of disease of the arteries. Many would part company with him in this opinion.

In the discussion of symptoms it is pointed out that arteriosclerosis is to be regarded as a by-product of many diseases, and cannot be represented as a "specific symptomatic series." We are not able to say that its morbid anatomy is uniform. The chapter on arteriosclerosis and the kidneys discusses perhaps the most involved aspect of the subject. Chapters on the myocardium in arteriosclerosis, diagnosis and prognosis, and treatment conclude this section. There is so much detailed notice of many points that space forbids mention of them.

*Angina Pectoris.* The discussion of this is preceded by a chapter on aortitis, and very properly so in view of the author's views on angina, which he holds is the result of disease of the aorta, especially of the part just above the aortic valves. In the discussion of aortitis the etiological importance of certain of the acute infectious diseases is properly emphasized. The frequency of acute aortitis in rheumatic fever, for example, is usually not recognized; it is



common in children who have aortic endocarditis. In septicemia it will often be found if looked for. Excluding the cases due to acute infection the author lays great stress on syphilis. It is not very clear exactly what proportion of the cases he regards as luetic. The reviewer inclines to the belief that there are many cases in which syphilis does not play any part, in this regard chronic aortitis being decidedly different from aneurysm.

The various theories of the cause of the pain in angina are discussed in detail. The author holds firmly to the opinion that the first portion of the aorta is concerned and that the cause is tension of the outer coat. He does not regard disease of the coronary arteries as the cause of the essential phenomena of angina. Professor Allbutt has often insisted on the proper use of words, and finds excellent examples of the importance of this in his discussion of angina. He points out the many inaccurate statements as to the seat of pain which is described as being cardiac, precordial, or submammary when it is really substernal. The discussion of the character of the pain in angina is most illuminating. If we accept his views many of the difficulties connected with the disease disappears. Much interest attaches to the discussion of the simulations of angina; the term pseudo-angina is dismissed from consideration. These chapters are important in clearing away preconceived erroneous notions. In the discussion of the theories of angina, there are some hard knocks to fanciful ideas. Professor Allbutt certainly has made out a strong case for the aortic origin of the symptoms.

The chapter on the diagnosis of angina is a short one, as so much of the discussion of this aspect is gone over in considering the symptoms. The occurrence of pain from cardiac disorder is discussed and the distinction from angina emphasized. The diagnosis seems a more simple matter to the author than it does to the majority of the profession. There is a group for the diagnosis of which time is often necessary, but it is wise to regard them as serious until proved otherwise. The view of prognosis is perhaps more cheerful than that of the majority of writers.

It is not easy to review this book in proper proportion; a review could be written on each chapter. The literature has been extensively noted and clear accounts of cases given to illustrate special points. It is not necessary to speak of the author's style; it is too well known to require comment. There are few medical works which will give more pleasure in the reading than this, and the reviewer very heartily advises it, both for pleasure and profit. You will not agree with all the views expressed, but you will read with interest in any case. To write a treatise on two of the most obscure subjects in medicine and make it full of interest is somewhat of a task. We believe that this work will take a high place in the literature of medicine, and Professor Allbutt has placed the profession in his debt for this splendid clinical treatise. T. McC.

INFECTION AND IMMUNITY. A TEXT-BOOK OF IMMUNOLOGY AND SEROLOGY. FOR STUDENTS AND PRACTITIONERS. BY CHARLES E. SIMON, B.A., M.D., Professor of Clinical Pathology and Experimental Medicine at the College of Physicians and Surgeons, Baltimore. Third edition. Pp. 351; 21 engravings and 12 plates. Philadelphia and New York: Lea & Febiger, 1915.

ORIGINALLY intended as an introduction to the study of infection and immunity and as a ground-work for more intensive and advanced study, this book of Dr. Simon's has been so enlarged that this the third edition might well serve as a text-book for students in a course of immunology. Moreover, the book will be found sufficiently large and amply comprehensive to serve the purpose of those practitioners who are interested in the practical side of the subject in its application to clinical problems. Lastly, as it has been written primarily for the general practitioner, the work will prove of inestimable value to the medical man who wishes a thorough grounding in the theoretical side of the subject even if he lacks the facilities to prepare the various laboratory tests as outlined by the author.

In the present edition the section on the Wassermann reaction has been greatly enlarged and so augmented that it will meet all requirements for the comprehension and performance of this important diagnostic aid. The Abderhalden test with complete technic have been incorporated in the text. The Schick test is carefully discussed, as is the production of antianaphylaxis. These are but a few of the many additions made in the new volume, but they will indicate, to a certain extent at least, how thorough and complete has been the revision.

*Infection and Immunity* can be most heartily recommended to the profession as a splendid reference and text-book on a subject which has only developed within a comparatively few years.

J. H. M., JR.

BONE-GRAFT SURGERY. BY FRED. H. ALBEE, A.B., M.D., F.A.C.S., Professor of Orthopedic Surgery at the New York Post-Graduate Medical School and the University of Vermont, etc. Pp. 417; 332 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

DR. ALBEE has been for some years an indefatigable enthusiast in advocacy of what he terms "bone-graft surgery," and he has now succeeded in accumulating enough material to write a book about it. This is not meant to imply that the subject is not worthy of being recorded in book form, nor to incline anyone to underestimate the value of transplantation of bone in general, but merely to suggest that a little more conciseness of statement and a little

less repetition of steps in technic would have rendered the volume more readable as well as none too small. As it stands now there is too much "padding;" the book has not received the editing which is its due.

The volume opens with chapters on fundamental principles and on the author's electric-motor outfit. There follow chapters devoted to the use of bone transplants in spinal affections, in fractures, in fixation of the larger joints, and in various miscellaneous affections such as club-foot, infantile paralysis, and after excision of the diaphyses of the long bones for osteomyelitis or tumors.

Some people have objected to Dr. Albee claiming so much credit for his work. They point out that there were heroes before Agamemnon, only they didn't blow so loud a trumpet. Now very likely this is true; but the fact remains that the man who popularizes, not to say exploits, a method of practice deserves very great credit for his exploitation, if for nothing else. This was the case of Gouley with the tunnelled catheter, of Freyer with suprapubic and of Young with perineal prostatectomy, and of Murphy with arthroplasty. It is true, of course, that many surgeons before Albee transplanted bone, and that his electric-motor outfit is only a modification of the Hartley-Kenyon motor, and that these latter gentlemen did not themselves invent electricity; and it is true that Hibbs was as early if not an earlier advocate of bone transplantation for spinal caries, and that even Albee's favorite "inlay method" was described in print in a leading article by Buchanan before (as much as one month before) Albee, in the closing paragraphs of a long paper, made rather incidental reference to the same method as used by himself. But if Buchanan can afford to ignore any claims for priority, why should anyone else object? Albee has established the method on a firm basis, and by his large experience in all varieties of bone transplantation has become a recognized authority. Wherefore, it is entirely fitting that he should publish a book on the subject.

What may perhaps be regarded as a just objection is that he permits his enthusiasm for bone transplantation to warp his judgment respecting the value of other and simpler surgical procedures. Like many other writers in recent years he blames all the bad results (and there are a great many) following the use of metal plates on the metal plates instead of on their inefficient use or on the lack of judgment and knowledge in the surgeon who employed them. There can be no question in the mind of anyone with sufficient experience in such matters that *metal plates are perfectly satisfactory for the treatment of recent fractures when properly applied*. Another criticism which we believe is just, is that Dr. Albee often strains at a gnat and finds he has swallowed a camel. Opening the volume at random just now, an instance of this greets the eye (p. 335): "Astragalus used as transplant to arthrodesis ankle"

is heralded as an epoch-making contribution to surgery; what was actually done was to produce ankylosis in the ankle and subastragalar joints by removing the astragalus and reimplanting it after properly denuding its articular surfaces and those of the neighboring bones. Now such an operation is currently done by orthopedic surgeons without disturbing the astragalus from its bed at all: the result is quite the same, and the procedure is much simpler.

But allowing for such shortcomings, due to acquired mental astigmatism, and ignoring carping criticisms, the volume remains an admirable record of work well done—an example for others to emulate.

A. P. C. A.

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GYNCOLOGICAL OPERATIONS, INCLUDING NON-OPERATIVE TREATMENT AND MINOR GYNCOLOGY. By HENRI HARTMANN, SC.D., Professor of the Faculty of Medicine, Paris; Surgeon to the Laennec Hospital, Paris; Member of the Society of Obstetrics and Gynecology; Member of the Society of Surgery; Member of the International Society of Surgery; Former President of the French Congress of Gynecology; Honorary Fellow, Clinical Society of London; Honorary Fellow, Royal College of Surgeons, Ireland. Translated by DOUGLAS W. SIBBALD, M.B., CH.B. (Edin.), formerly Physician to the British Hospital, Levallois-Perrot, Paris. 422 illustrations. Philadelphia: P. Blakiston's Son & Co., 1913.

THERE can be no doubt that a translated work often loses much of its value in the process of translation, since the literary style of the author is not easily expressed in a foreign tongue. In the work under consideration the translation has been done in a very mediocre manner, perhaps on account of the effort of the translator to stick too closely to the original text. The English construction is very poor indeed, errors in spelling are common, and there are many evidences of carelessness in proofreading. The illustrations do not approach the standard which we have become accustomed to expect in works of this character, most of them being made from wood-cuts. A redeeming feature of the book is the fact that the type is large and very easily read. Although, as the title indicates, the book is intended to be a dissertation on the operative side of gynecology, with no attention given to symptomatology, considerable space is devoted to non-operative therapy and minor gynecology, the subject of electrotherapy being well handled by Zimmern. Many of the procedures advocated by Hartmann as methods of choice are seldom employed in this country today, such as dilatation of the uterus by means of laminaria tents and morcelllement in the treatment of uterine fibroids. Curettage is discussed at length,

the author favoring its use in septic abortions. The best articles in the book are those devoted to hysterectomy, each of the more prominent methods of performing this operation is considered in turn, followed by the various modifications of these methods, concluding with the indications, contra-indications, and complications in each case. This part of the work, especially the chapter on vaginal hysterectomy, is well illustrated. The disorders of menstruation are mentioned in a very superficial way; chapters on the urinary organs, especially the treatment of the various urinary fistulæ, are most satisfactory. The book contains much information, but needs considerable polish and revision. F. E. K.

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DIARRHEAL, INFLAMMATORY, OBSTRUCTIVE AND PARASITIC DISEASES OF THE GASTRO-INTESTINAL TRACT. By SAMUEL GOODWIN GANT, M.D., LL.D., Professor of Diseases of the Colon, Sigmoid Flexure, Rectum and Anus at the New York Post-Graduate Medical School and Hospital. Pp. 604; 181 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

As a corollary to his recently published work on constipation, Dr. Gant has brought out a book on the adverse condition, diarrhea, which follows very much on the same lines the plan pursued in the original work. The book is an extremely careful compilation of all the various types of primary diarrhea, that is, the diarrheas that occur as a result of intestinal diseases and of the manifestations of diarrhea that occur in conditions which have no direct relationship to the intestines. As would be expected in a book of this type, the major part of the text is devoted to treatment which includes not only drug therapy, but also mechanical treatment, and treatment by operative procedure; to this last method of treatment incidentally some fifty pages are devoted. However, the other phases of diarrheal diseases are not neglected by any means, so that the work will prove a splendid reference book upon a protean subject. J. H. M., Jr.

THE MEDICAL CLINICS OF CHICAGO. Vol. I, No. 4, January, 1916. Pp. 221; 23 illustrations. Philadelphia and London: W. B. Saunders Company, 1916.

THE fourth number of the *Chicago Medical Clinics* opens with an excellent discussion of epidemic cerebrospinal meningitis by Dr.

Tice. In the clinics devoted to this subject he details the technic of lumbar puncture and the examination of the cerebrospinal fluid in a most thorough and careful manner. The next two clinics by this author deal with Pick's cirrhosis and with acute endocarditis complicated by meningitis.

Dr. Hamburger follows with an equally good exposition on primary carcinoma of the liver, the pathological side of which is discussed by Dr. Kuh.

Dr. Weaver then gives a most pertinent talk on the Schick reaction.

In Dr. Mix's presentation of a case of upper lobe pneumonia he lays particular stress, as prognostic signs, upon accentuation of the pulmonic second sound, the relation between pulse-rate and blood-pressure, and the occurrence of arrhythmia. The first of these is undoubtedly of some prognostic value, the second is an extremely doubtful prognostic sign. Opinion varies considerably concerning the value of Gibson's rule, but certainly most clinicians doubt its prognostic worth. As to the question of arrhythmia, the type or types of arrhythmia which lead to fatal result in pneumonia are not specified. Hundreds of children recover from pneumonia who have had well-marked sinus arrhythmias during the course of the disease.

Dr. Hamill's neurological clinics, which are next in order, are carefully prepared and interestingly presented.

Cases of malaria, hemorrhagic pleurisy and trichinosis are shown by Dr. Williamson in his clinic.

Dr. Preble's bedside clinic is spoiled for the reader by entirely too much questioning and subsequent answering by the "visitor."

Dr. Goodkind's contributions are a case of pneumococcic cerebrospinal meningitis and a case which is called aplastic anemia but which lacks many of the characteristics of this type of anemia. The author evidently is not sure of his diagnosis in this case because he says in the text that he is justified in saying that the diagnosis is pernicious anemia of the idiopathic type.

La grippe in infants, a clinic by Dr. Alt, which is well worth reading, concludes the present number of the *Clinics*.

J. H. M., JR.

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MANUAL OF EMBRYOLOGY. By A. MELVILLE PATERSON, Professor of Anatomy in the University of Liverpool. Pp. 391; 304 figures. New York: Oxford University Press, American Branch, 1915.

In this printed version of his lectures on embryology the author has succeeded in reducing to a compact and easily understandable form the important facts of his subject. It will be useful to all who wish a definite answer to questions concerning the prenatal history of the organs and systems. The author's style is terse and lucid,

and the book is illustrated with numerous diagrammatic figures, which help much to elucidate the text. Many of these are adapted from previous works, but the author has also evolved a number of original ones. Everywhere the history of the organs leads up to the fully formed condition, and for that reason will appeal especially to those whose acquaintance is with gross rather than with microscopic anatomy. The keynote of the book is evidently clearness and simplicity. This, of course, has the disadvantage of preventing discussion of controversial points, and makes some of the statements unduly hard and fast. However, for the beginner or for the man whose laboratory instruction in the subject has only been elementary, this form of manual will be very welcome.

W. H. F. A.

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PRACTICAL CYSTOSCOPY AND THE DIAGNOSIS OF SURGICAL DISEASES OF THE KIDNEYS AND URINARY BLADDER. By PAUL M. PILCHER, M.D., Consulting Surgeon to the Eastern Long Island Hospital. Second edition, thoroughly revised and enlarged. Pp. 504; 299 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

A DETAILED review of this second edition of Pilcher's book might well be compared to the introduction of old friends who had merely modified their garb to suit a more modern style. Four years have elapsed since the first edition was published, and during this time the book has become well and favorably known. The general arrangement of the first edition remains unchanged, one or two new chapters have been added, and others amplified or altered to embody the more recent developments. The chapter on pyelography is new, and is a concise statement of facts concerning its indications, value, technic, and dangers. At the conclusion of this chapter are pyelograms, furnished by Braasch, demonstrating the various types of renal lesions. The chapters on diseases of the prostate and functional diagnosis have been entirely rewritten; under the latter heading only the more generally used and accepted tests are described in full, the others being mentioned but passed by with a few words. We do not agree with the author's general statement that the phthalein test "is interfered with by parenchymatous nephritis, but does not seem to be influenced by chronic interstitial nephritis." The latter portion of the book details the therapeutic uses of the cystoscope and the application of the high-frequency current in various diseases of the bladder and ureter.

This book while intended primarily for the specialist must appeal to the man in general work as well, taking up as it does the clinical history and diagnosis of the various diseases of the urinary system.

It can be recommended as a practical, up-to-date presentation of the entire subject.

F. E. K.

HANDBUCH DER TUBERKULOSE. Edited by PROF. DR. L. BRAUER, Hamburg-Eppendorf, Allg. Krankenhaus, Dr. G. SCHRÖDER, Dirigierender Arzt der neuen Heilanstalt f. Lungenkranke zu Schönberg, O. A. NEUBÜRG und Dr. F. BLUMENFELD, Arzt f. Nasen, Hals- und Lungenkrankheiten in Wiesbaden. Vol. I (in two sections). Pp. 792; 88 illustrations; 18 plates. Leipzig: Johann Ambrosius Barth.

THE first volume of the five comprising this system is divided into two sections, the first dealing with the history, pathology, and epidemiology of the disease, and the second covering diagnosis.

The articles are so comprehensive and cover the subject so thoroughly and in such detail that it is very difficult to select any articles for special consideration. The pathological anatomy of tuberculosis is covered by Tendeloo in an article containing a wealth of information illustrated by carefully selected plates. This subject is so important for a thorough understanding of the disease that it deserves special mention, although it is unfortunate that this chapter is not brought into closer relation to the chapter dealing with the study of the clinical types (Meissen, second section), as it would have materially added to the value of each.

Much's article on the tubercle bacillus is largely devoted to a presentation of the writer's views in regard to the significance of the granular rods and granules which he has described, a long list being given of the writers who have supported his views and a few whose investigations failed to confirm his findings.

The various theories held in relation to infection, especially infection in childhood, have been very carefully reviewed in the article by Römer. Much's article on immunity, Gottstein's on epidemiology, and Dammann's on the prevention of tuberculosis in animals add considerable value to this volume as a work of reference.

The second section will probably have a more general interest among clinicians, especially the article on diagnosis by Brecke which is exceptionally good.

In view of the fact that the study of the temperature as an aid in diagnosis is usually ignored both by writers and clinicians, it is worthy of note that the portion of the article dealing with this subject is very complete, containing a review of numerous studies and several observations by the writer. The portion dealing with the history of the patient seems to be unnecessarily brief.

The articles by Ritter, on the clinical significance of the tuberculin reactions, and by Lorey, on the use of the roentgen-rays, are very thorough and exhaustive presentations of the respective subjects, although the claims made for the roentgen-rays, as is so frequently the case, seem rather extravagant.

Thoracoscopy and laparoscopy as described by Jacobaeus, as a



means of diagnosis, will probably never be very widely adopted by clinicians in this country.

This system, if the succeeding volumes maintain the standard set up by this volume, will be of value to the general clinician mainly as a work of reference, while those especially interested in the study of this disease will find it invaluable. It is especially unfortunate that in a work containing such a wealth of information of an accurate and scientific nature the material should be so inaccessible on account of the lack of systematic grouping and arrangement of the text, a failing so common to works of German origin. The references alone make the work valuable, although the references to English and American writers are conspicuous by their rarity.

F. A. C.

PHARMACOLOGY, CLINICAL AND EXPERIMENTAL. A GROUNDWORK OF MEDICAL TREATMENT. By H. H. MEYER and R. GOTTLIEB, Professors of Pharmacology at Vienna and Heidelberg. Translated by J. T. HALSEY, Professor of Pharmacology, Therapeutics, and Clinical Medicine at Tulane University. Pp. 604; 64 illustrations. Philadelphia and London: J. B. Lippincott & Co.

CONSIDERING pharmacology as the "reaction of living organisms to various chemical agents," the authors have made an able presentation of scientific drug therapy, with frequent references to physiology and the seat and cause of the pathological conditions involved. As its name implies their book is more than a text-book of therapeutics in that it considers the pharmacological action of certain drugs not used in medicine (*e. g.*, curare, the first drug discussed). On the other hand it does not attempt to include remedies other than drugs, such as massage, electricity, baths and so forth.

A fundamental division of all drugs is made into two classes: organotropic (drugs influencing organs and their functions) and etiotropic (those acting on the causative agents of disease). The table of contents is divided into eighteen chapters, the first fourteen being devoted to the pharmacology of the several organs; the last four to the pharmacology of heat regulation, of inflammation, etiotropic pharmacological agents, and factors influencing pharmacological reactions. Drugs are not considered individually, but under each organ that they affect pharmacologically. A comprehensive list of original sources is given at the end of each chapter. All doses are given in the metric system only.

Numerous additional facts and opinions are inserted in brackets by the translator. These so frequently disagree with the authors, and sometimes supply such serious omissions, that an original

work by the translator would be awaited with interest. For example, the important effect of digitalis on the conductivity of the heart, so well demonstrated by Mackenzie, Cushny, and Lewis, is briefly dealt with between brackets on page 266.

The subject matter appears on the whole to be accurately and adequately given. Many of the newer synthetic compounds are given, with cautious estimation as to their probable worth. Among the cathartics the phthaleins are emphasized, including the phenol-tetrachlorophthalein as advocated by Abel and Rowntree. One is surprised, however, to find no mention of agar-agar or paraffin oil among the laxatives.

The book is well bound and well printed on good paper, and misprints are few. A dangerous slip occurs on page 38, where 0.02 gm. of pantopon is said to correspond to 0.1 gm. of morphin instead of 0.01 gm. morphin.

E. B. K.

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SELECTED ADDRESSES. By JAMES TYSON, M.D., LL.D., Professor of Medicine Emeritus, University of Pennsylvania. Pp. 366. Philadelphia: P. Blakiston's Son & Co.

THE fifteen addresses collected in this volume were made by Dr. Tyson on various occasions between the years 1884 and 1910. There are also included three articles descriptive of European spas.

The addresses cover a wide range of subjects: education, biography, travel, and medicine. Noteworthy are those on college education, which contain much that is descriptive of Dr. Tyson's undergraduate life at Haverford College.

The presidential address at the dedication of the new hall at the College of Physicians of Philadelphia is of particular interest by reason of the many references to the early medical history of this country.

The work is carefully edited, and the addresses from first to last are written in the scholarly manner which has always characterized Dr. Tyson's literary contributions.

This volume should be of particular interest to his former pupils, of whom some six thousand have been graduated during his connection with the Medical School of the University of Pennsylvania.

R. G. T.

# PROGRESS OF MEDICAL SCIENCE

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## MEDICINE

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UNDER THE CHARGE OF

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**Indicanemia.**—HAAS (*München. med. Wchnschr.*, August 3, 1915) calls attention to the diagnostic importance of an increase in indican in the serum. It was first recognized by Obermayer and Popper, who found that indican was practically never present in the serum except in uremia, in which condition it is always found in greater or less amounts. The author states that it is often present not only in uremia, but also in chronic nephritis of all types and it is not confined to those cases showing a nitrogen retention in the blood. It is a better sign of renal insufficiency than increased rest nitrogen.

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**Concerning Septic Meningococcus Infection.**—BITTORF (*Deutsch. med. Wchnschr.*, 1915, No. 37) cites four instances of meningococcus infection with all the characteristics of a general septicemia and with the recovery of the meningococcus from the blood in one case. He regards the disease as a general septic infection in which the meningitis constitutes only one feature of the general picture and is due to organisms brought by the blood stream rather than the usual view that it is secondary to direct invasion from the naso-pharynx. The following points are offered in support of his view that the meningitis is only a part of the picture of a general septicemia: (a) The presence of a typical septic embolic eruption with the early round or oval dark-blue spots in the skin which later become definitely infiltrated and in some instances go on to pustule formation. (b) Numerous septic metastatic symptoms, oftenest multiple, swollen and painful joints, endocarditis and in one case hemorrhagic nephritis. (c) The appearance of an acute splenic tumor in three out of the four cases. (d) Septic temperature with chills and jaundice. (e) The recovery of the organism from

from the blood in one case. In all cases the meningococcus was recovered from the spinal fluid and the possibility of a myeloid infection to account for the general septic picture presented by these patients was excluded from the onset. The appearance of meningitis later in the course of the disease has only the same significance as the joint and skin manifestations. This is further supported by the finding of only a very few organisms and a moderate cellular increase in the early lumbar puncture, but with a marked increase in both elements in the fluid withdrawn later. These observations agree with those of Ostermann (1906 and 1907) who considers the disease a hematogenous infection with the portal of entry in the naso-pharynx while the tonsils seemed the more likely source in these cases. The cultivation of the organism from the blood has also been previously reported by Westenhoeffer, Salomon and Martini, and Rhode. All the cases reported recovered from the meningitis (one died suddenly during convalescence) with the use of frequent lumbar puncture, large doses of salicylic acid and urotropin when the meningitic symptoms started. Antimeningitis serum was not used in any case.

**The Use of Brain Extracts as an Antigen in the Wassermann Reaction.**—MARUYAMA (*Jahrb. f. Psych. u. Neur.*, 1914) has taken up the question as to whether extracts of parietic brains would serve to give specific complement fixation in the Wassermann reaction. He made various types of extracts, such as plain alcohol, alcohol ether and acetone, and tested all of these antigens against a rather wide variety of cases, both luetic and otherwise. Though the series is but small, and in the author's opinion warrants no positive conclusions, he has felt justified in arriving at the following facts: (1) Alcohol and alcohol ether extracts of brain substance are of no use as antigens in the Wassermann reaction. (2) Acetone extracts, however, seem to give results of a very valuable and specific nature in the Wassermann reaction. The question remains open as to whether these antigens contain an unusual amount of cholesterol or not, but he is rather inclined to believe that they do. In only one case did he note a negative result with the acetone extract in a case where the blood serum gave a positive reaction when tested with the usual type of antigens. A number of suggestive leads are opened up by this study which may be of service in throwing more light upon the nature and specificity of this much used reaction.

**Concerning the Function of the Spleen.**—After reviewing the various ancient theories and more recent knowledge of the function and importance of the spleen, HIRSCHFELD (*Deutsch. med. Wchnschr.*, 1915, Nos. 37 and 38) feels that the same relation between the organs of blood building and blood destruction exists as between the various glands of internal secretion. The profound disturbance of erythropoiesis in the bone marrow following the loss of function can scarcely be explained except on the basis of an interacting internal secretion. The present state of our knowledge concerning the function of the spleen, he summarizes as follows: (1) The human spleen is a blood building organ. In the normal person it is not concerned in the building of red cells but is a factor in the production of lymphocytes and

large mononuclears. Under certain pathological conditions, such as leukemias, anemias and infectious diseases, the spleen can take on the function of building all the blood elements. (2) Normally the red cells are destroyed in the spleen and the hemoglobin starts there the subsequent change into bilirubin in the liver. It thus plays a helpful part in conjunction with the liver in hemoglobin metabolism. (3) It is one of the organs concerned in the iron metabolism which substance it can store and thus help maintain the hemoglobin content of the body at its normal element. (4) It acts as a lymph gland and is not only a burial ground for the red cells but for the white cells and any foreign substance circulating in the blood. The latter accounts for the well-known changes in the spleen seen in infectious diseases. It is also one of the places for the building of immune bodies against bacteria. (5) It is a regulator of the erythroplastic function of the bone marrow. Splenectomized animals and men show in the circulation red cells containing Howell-Jolly bodies, a symptom of disturbed erythroblastic regeneration. In occasional cases this disturbance leads to a true polycythemia. (6) None of the functions of the spleen are vital, as they are often very quickly taken over by other organs and the patient lives normally after extirpation of the spleen, without any disturbance in health. (7) For most individuals the spleen is unnecessary. Yet there are people in whom splenectomy leads to a definite and severe disturbance with polycythemia.

## SURGERY

UNDER THE CHARGE OF

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**Clinical Results of 1000 Intravenous Injections of Galyl.** SPENCE (*Lancet*, December 11, 1915, p. 1292) says that no systematic study has been undertaken of the effect of the injections on the Wassermann reaction or of certain other questions chiefly of academic interest. Galyl, or tetraoxydiphosphaminodiarsenobenzene, is one of several synthetic substitutes for salvarsan which have recently appeared on the market. A comparison of the full doses advised for galyl and for salvarsan and neosalvarsan indicates that galyl as administered actually contains only about half as much arsenic as the others, a point of passing interest in view of the recent suggestion that the activity of these agents may be not wholly dependent on the arsenic moiety.

The preparation is supplied in five different strengths—viz., 0.4 gm., stated to be the full dose and to correspond to 0.9 neosalvarsan; three smaller, 0.25, 0.30, and 0.35 gm.; and a larger, 5 gm. It is left to be inferred that the large dose is to be used only very occasionally, or in other words that it is a specially powerful one. It is used in precisely the same way as neosalvarsan, either in concentrated solution in the 10 c.c. piston syringe, or more dilute in the familiar burette apparatus, preceded and followed by a little distilled water. A perusal of the histories will at once suggest that in clearing up symptoms the new preparation differs little if at all from its older rival. Second only in importance to effectiveness in clearing up symptoms is the question of toxicity. More than 150 deaths are credited to salvarsan, to say nothing of innumerable accidents and severe reactions. So far as Spence is aware no fatality has as yet been reported with galyl. Neither has there been reported any undoubted case of arsenical intoxication, but in this connection it is to be remembered that the remedy is new and its literature very meagre. An interesting complication met with twice was a reaction resembling serum sickness, large urticarial wheals which itched intensely, appearing a few hours after administration and remaining two or three days. Seven cases exhibited a pseudo-Herxheimer reaction, all the symptoms seeming to be temporarily aggravated, the throat more congested and painful, and rash and malaise accentuated. It is, however, but fair to say that any one of the reactions and symptom just enumerated is at least as frequent with salvarsan and neosalvarsan, and none is typical of arsenical poisoning, very probably being due, as the studies of Yakimoff and others indicate, to the release of various bacterial endotoxins.

**Intestinal Stasis.**—OCHSNER (*Surg., Gynec. and Obst.*, 1916, xxii, 44) says that during the year ending December 31, 1914, operation to correct intestinal stasis was performed on 36 cases, with 32 recoveries and four deaths. These cases represent less than 10 per cent. of all the cases examined during this period, and treated for intestinal stasis, and still the number operated upon contains some cases which should not have been treated surgically, as has been shown by their subsequent condition. This is true especially of a few neurotics who undoubtedly suffered as a result of intestinal stasis with marked auto-intoxication due to absorption of products of decomposition. All of these neurotic cases showed marked improvement after operation. In a certain proportion, however, this seemed to last only until some unusual or unexpected circumstance upset the regularity of the digestive process, when they seemed to glory in the consciousness that they were again enjoying a type of ill health which they could attribute to the abnormal condition of the intestinal tract. In some of these cases a second or third operation was performed, but only rarely with the result of obtaining permanent relief. There can be no doubt but that the surgical relief of demonstrable mechanical obstruction causing stasis will in many instances give complete or almost complete relief, the result depending upon the degree to which the stasis is due to a removable mechanical obstruction. In a very large proportion of the cases, however, the cause is not single and for this reason one should look for only partial relief following surgical treatment. Only a very small

percentage of patients suffering from intestinal stasis will need to be considered from the surgical standpoint. This applies to those in whom there is a possibility of overcoming intestinal stasis by removing the cause of the obstruction existing in the form of tumors pressing upon the intestine, the correction of uterine displacement compressing the rectum, obstruction due to bands of adhesions, or marked kinking of intestines, of strictures due to cicatricial contraction following ulcer of the intestine, of annular carcinoma of the intestines and occasionally of large papillomata, fibromata, or lipomata projecting into the intestine. If for any reason the obstruction cannot be relieved in this way then short circuiting must be resorted to, and if the colon is dilated with its muscular walls so seriously impaired that the power of contraction has been permanently destroyed, then at least the cecum and ascending colon should be removed; and in severe cases it may become necessary to remove the entire colon down to the sigmoid flexure.

**The Abdominal Skin-flap in Radical Amputation of the Breast.**—ELSBURG (*Ann. Surg.*, 1915, lxii, 678) says that the abdominal skin-flap is necessary only in those cases in which the defect left after radical amputation of the breast cannot be closed by any of the methods ordinarily in use; it is useful after extensive removal of the skin and makes skin grafting unnecessary. The skin of the abdominal wall is generally very lax and receives abundant blood supply from branches of the arteries which run through the wall of the abdomen from behind forward. If the base of the skin-flap is not too small the tissues will be well supplied with blood, and there is no danger of sloughing or of marginal skin necrosis. After the flap has been raised from the fascia and slid upward into a new position, there is no difficulty in closing the defect in the abdominal wall with interrupted sutures. It is surprising how much skin can be used for the flap and sufficient remain to close up the defect in the abdominal parietes without much tension. The size and shape of the abdominal skin-flap will depend upon the size and shape of the raw surface on the chest wall.

**Operation for Relapsed Club-foot.**—Cook (*Amer. Jour. Orthop. Surg.*, 1916, xiv, 9) presents the following description of the operation which, in his personal experience, has proved the most useful for relapsed club-foot in cases that have resisted the ordinary methods of treatment. There is no age limit, no preliminary treatment and no after-treatment beyond the time required for the healing of the wound. (1) If necessary subcutaneously divide the fascia on the inner side of the foot and also the heel cord; then bring the foot into as good position as possible, using nothing but the hands and being careful not to bruise the tissues. (2) Make an incision through the skin and superficial fascia just in front of the external malleolus on the outer side of the foot. The skin incision should be perpendicular from the bottom of the foot to just above the bend of the ankle. (3) With an osteotome remove a large wedge of bone; make the first incision far back, just in front of the fibula. Pay no attention to the periosteum or peronei tendons. Cut the bones completely across and remove everything. Be sure to make the wedge large enough. The foot can now be brought without force into excellent position, and by giving the anterior part

of the foot a quarter turn, its outer border can be elevated. It is vitally essential to the success of the operation that the outer border of the foot be elevated. In order to do this the tarsus is cut completely across to enable the operator to give the anterior foot the quarter turn which elevates the outer border. Cook uses a light retention splint in preference to a plaster cast. Young children often walk at the end of two weeks. He has been doing the operation for the past twenty years, and during the last three and a half years exactly as described above, operating on 30 patients in all, in some cases on both feet. Three of the feet have relapsed and a secondary operation was necessary, probably, because a sufficiently large wedge of bone was not removed in the first place. All of the patients are cured and all have practically perfect functional use of their feet.

**Technic of Thyroidectomy.**—QUERVAIX (*Deutsch. Ztschr. f. Chir.*, 1916, cxxxiv, 475) says that he has worked up a technic for goitre operations which he has employed for five years, and the chief points of which are as follows: He ligates the arteries, especially the inferior thyroid, when it does the most good, before the gland is luxated. The ligation of the usually well developed inferior thyroid should be extrafascial, outside of the gland fascia derived from the cervical fascia, because one can avoid most surely here the structures inside of the gland fascia, the recurrent laryngeal nerve and the parathyroids, as well as the capsule veins. The best approach is afforded by the sternohyoid space, *i. e.*, the space in which the small thyroid gland muscles are found, and best to the outer side of these muscles but inside of the strong fascia covering them. Whether the goitre tissue is to be removed by enucleation or resection will depend upon the form of the goitre and has no special importance. The isthmus is to be divided and partly or wholly removed, only when it is itself diseased. In all other cases its division is superfluous and a disadvantage, because the collateral vessels at its upper and lower borders are damaged. These to some extent provide nourishment to the stump after the ligation of both arteries of one side. Whenever possible, as much of the gland is to be left on each side as corresponds to the normal gland lobe. The posterior surface of the lobe and, therefore, the region of the recurrent laryngeal nerve and parathyroids, will remain untouched and neither of them will be exposed. The parenchymatous hemorrhage will be controlled by a fine catgut suture which unites the two edges of the defect remaining in the gland.

**Studies on the Localization of Cerebellar Tumors.**—GREY (*Ann. Surg.*, 1916, lxiii, 129) reports a study from the surgical clinic of the Peter Bent Brigham Hospital, Harvard Medical School, with particular reference to the position of the head and suboccipital discomforts. Of 58 certified cases of cerebellar and extracerebellar tumor an unusual attitude of the head—tilted so that the ear approximated one shoulder, or both—was found in 23. In the majority of these the change in position was slight. Of 13 certified cases of tumor lying anterior to the cerebellum only 3 showed any tilt or rotation of the head. The unusual attitude in these 3 cases was scarcely noticeable. About 40 per cent., then, of the cases with cerebellar tumor showed some change in the



position of the head while only 7 per cent. of the cases with tumors anterior to the cerebellum showed any unusual attitude. These findings indicate that a tilt or rotation of the head in a patient with symptoms pointing toward an intracranial tumor is suggestive of a subtentorial newgrowth. Such an attitude, however, has no additional significance in localizing the lesion in one or other side of the posterior cranial fossa. Backward retraction of the head was a feature in 8 of the 60 cases of cerebellar and extracerebellar tumor. Typical opisthotonos attacks appeared in 2 of these. A similar position was noted in none of the cases with tumors lying anterior to the cerebellum. Backward retraction of the head, then, is characteristic of newgrowths situated below the tentorium. While atrophy or osteoporosis of the subjacent bone may occasion occipital tenderness in certain cases, comparisons of the clinical and operative findings in this series of cases have shown no consistent relations to exist between the two. Of 59 certified cases of cerebellar and extracerebellar tumor some form of suboccipital discomfort was present in 44, about 75 per cent. Tenderness in the occiput was found in 21, 36 per cent. Suboccipital headache or pain was complained of in 33, 56 per cent. There was more or less soreness or stiffness of the neck muscles in 18, nearly 31 per cent. Accordingly, headache or pain is the most frequent of the suboccipital discomforts. Of 43 certified cases with tumors lying anterior to the cerebellum some degree of suboccipital discomfort was found in 14, approximately 33 per cent. Suboccipital tenderness was present in 8, nearly 19 per cent. Suboccipital headache or pain appeared in 10, about 23 per cent. Soreness or stiffness of the neck muscles was complained of in 6, 14 per cent. As a rule the occipital discomforts were much less intense in the cases with tumors situated anterior to the cerebellum than in those with subtentorial newgrowths. Taking the series as a whole, no consistent relation has been found between the part of the posterior cranial fossa occupied by the tumor and the site of the discomfort. When unilateral suboccipital discomfort is present, however, it is slightly suggestive of the site of the newgrowth. These findings indicate that suboccipital discomforts are present more than twice as often in patients with subtentorial newgrowths as in those with tumors situated elsewhere in the brain; and, though they afford only slight assistance in localizing the lesion in one or the other side of the posterior cranial fossa, they nevertheless rank with asynergy (limb ataxia, staggering gait, etc.) as the most important indications of a subtentorial localization of intracranial newgrowths.

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**Fractures of the Spine Without Paraplegia.**—HARTWELL (*Am. Jour. Orthop. Surg.*, 1916, xiv, 82) says that during a six months' service in the male surgical division of the out-patient department of the Massachusetts General Hospital—from February 1, 1915, to August 1, 1915—ten patients sought relief for pain in the back who were found to have a fracture of the spine. And during this same period one patient with spinal fracture was treated in the orthopedic division. These patients were all ambulatory, and attempts to elicit a history of symptoms that might indicate cord compression were vain. Not one had at any time had any motor or sensory paralysis or sphincteric disturbance. In a review of 133 cases of spinal fracture treated at the Massachusetts

General Hospital between January 1, 1900 and December 31, 1914, 106 patients were found to have applied for treatment within forty-eight hours of the receipt of the injury. Fifteen per cent. of patients with fracture in the cervical region, 32.4 per cent. of patients with fracture in the dorsal region, and 48.3 per cent. of patients with fracture in the lumbar spine, presented no signs of damage to the spinal cord. A study of the subject is summarized as follows: Fractures of the vertebral bodies and lumbar transverse processes are not infrequent injuries but are generally overlooked. These fractures cause steady pain in the back but need not be accompanied by any neurological symptoms. Localized tenderness over the spinous processes should always suggest the possibility of fracture of the spine, and if in addition to localized tenderness there is a disalignment of the spinous processes, the diagnosis is almost certain. The kyphos caused by compression fractures may readily be mistaken for the deformity of a bad posture. Treatment should consist of prolonged fixation of the spine in extension by plaster jackets or permanent splinting of the spine by a bone grafting operation.

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**The Physiological Treatment of Bullet and Gunshot Wounds of the Peripheral Nerve Trunks.**—*LYLE* (*Surg., Gynec. and Obst.*, 1916, xxii, 127) studied cases while in charge of an American Hospital in France. In the first 225 cases there were thirty-three nerve lesions. Of these, twenty-nine were injuries to the peripheral nerves. The musculospiral was involved 8 times, the median 4, the ulnar 6, the external popliteal 2, the circumflex 1, the musculocutaneous of the leg 1, the sciatic 1, the brachial plexus with sensory disturbances in the ulnar 1 time. Other lesions complicated the nerve injuries in some cases. He says that damage to an important peripheral nerve is an injury of extreme gravity. Primary nerve suture is rarely indicated in war time. Unrelieved, overstretched, muscular tissue leads to fatty degeneration and consequent loss of contractility. A paralytic deformity with shortened muscle and limited joint movement, in the majority of cases, is the result of ignorance or neglect. It is imperative, whether the nerve is divided or not, that the paralyzed muscles be relaxed and protected from strain by a suitable apparatus. Under no circumstances must this be deferred to the so-called after-treatment. The postural prophylaxis begins with the reception of the wound and continues after the operation until voluntary motion is restored. A strict adherence to this vital orthopedic principle aids in the diagnosis, hastens recovery, prevents many distressing deformities, and will materially diminish the number of useless limbs. This essential principle has not received the attention from the general profession that it deserves.

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**The Operative Treatment of Varicose Veins and Ulcers Based upon a Classification of These Lesions.**—*HOMANS* (*Surg., Gynec. and Obst.*, 1916, xxii, 143) says that varicosity of the veins of the legs is confined for anatomic and physiologic reasons to the superficial and perforating vessels. Trendelenburg's tests distinguish between pure surface varix and surface varix complicated by varicosity of the perforating veins, a distinction for purposes of treatment. Surface varix is curable by relatively simple surgical procedures, preferably excision of the great

saphenous vein from groin to mid-calf. Surface varix complicated by varicosity of the perforating veins requires for its cure not only eradication of the great saphenous vein but a thorough exploration of the lower leg in order to ligate varicose perforating veins. Varix following phlebitis is not uncommon, presents a characteristic appearance, is prone to be complicated by varicosity of the perforating veins, and is usually accompanied by obstinate ulceration soon after its establishment. It is a very general rule if not a law, that the more prominent and tortuous the surface veins the simpler the cure; the less noticeable the surface veins the more malignant and resistant their attendant ulcers, and the more radical the operative procedure required for cure. Varicose ulcers, if of long standing and especially if they are surrounded by an area of thick scar tissue, are best treated by free excision and immediate skin graft in connection with the radical removal of the veins to which they are tributary.

## THERAPEUTICS

UNDER THE CHARGE OF

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**The Therapeutic Action of Iodin.**—JOBLING and PETERSON (*Arch. Int. Med.*, 1915, xv, 286) give experimental and clinical evidence that indicates that the action of iodine in causing absorption of necrotic material is due to the lowering of the antitryptic action of the blood. They believe that the antitrypsin of the blood and tissues is the most important factor in preventing the resolution of necrotic tissues such as are found in infarcts and in the caseous areas in syphilis and tuberculosis. They demonstrated that the antitryptic action of the blood and of tuberculous caseous matter is due to the presence of unsaturated fatty acids. They then studied the antitryptic strength of the serum of patients to whom iodids were being given. They found that when iodids were administered a very considerable reduction in the antitryptic activity of the blood occurred. This decrease in antitrypsin permits the ferments normally present in the necrotic areas to become active and thus hasten autolysis. The authors believe that iodine combines with the unsaturated fatty acids, thus causing a neutralization of the activity of these substances as ferment-inhibiting agents. Jobling and Peterson state that there is a general impression among clinicians that iodids are harmful in tuberculosis, as they promote the spread of the infection by causing a softening of the tubercles and also interfere with connective tissue formation. They explain the well known clinical observation that iodids cause tubercle bacilli to appear in the sputum of patients though they were previously absent, by the fact that softened caseous matter ruptures into the bronchi. The softening

of the caseous tuberculous tissue is due to the autolysis induced by the iodine. Pulmonary hemorrhages may be explained in the same way. Clinical experience has shown that iodine is almost a specific in bringing about the amelioration of symptoms and the disappearance of lesions in syphilis, and yet little is known concerning the means by which these results are obtained. As experimental work and clinical observations have demonstrated that the iodides do not destroy the infecting organism we must assume, according to the authors, that the results obtained are due to the power the iodides possess of causing resolutions of the lesions. Their view is that iodine neutralizes the action of the agents which prevent solution and absorption of necrotic tissue, and at the same time lays bare to the action of the real germicidal agent the infecting organism which previously had been protected by necrotic tissue. With the exposure of the infecting organism such agents as mercury and salvarsan would be much more effective.

**Mouth Infection as a Source of Systemic Disease.**—ROSENOW (*Jour. Amer. Med. Assn.*, 1914, lxiii, 2026) says that abscesses or bony changes found about the roots of teeth in various systemic diseases, especially in cases of chronic arthritis, may or may not be primary, but if found the condition should be corrected because vaccine or other treatment largely fails so long as an active focus of infection exists. In the light of our present knowledge the argument that infections in the mouth are very common in individuals in apparent health, does not minimize their importance. Regarding autogenous vaccines, he says that our ideas need to be somewhat revised in view of the fact that the vaccines administered are usually prepared from streptococci in the focus which may or may not be the causative organism. The instances in which good results are obtained are probably those in which the focus harbored the causative organism. The poor results in some cases of arthritis following the use of autogenous vaccines prepared from the tonsils or other presumable focus, may be due to the fact that the organisms present in the focus at the time, were not the same as those actually infecting the tissues. In this case the vaccine would fail to contain the proper antigen and be ineffectual for therapeutic purposes. Rosenow says that he was able to isolate *Streptococcus rheumaticus* from the stools of two cases of typical rheumatism; in one from an infected ingrowing toe-nail, and in another case from the wound in the thumb following a crushing injury. He cites these as unusual foci of infection and in a given case the determination of a single focus of infection may not be enough to prove the causative factor of the systemic disease.

**The Use of Strychnin and Caffeine as Cardiac Vaso Stimulants in the Acute Infectious Diseases.**—NEWBURN (*Arch. Int. Med.*, 1915, xv, 458) says that for decades many physicians have relied on strychnin in the treatment of certain grave cardiac symptoms occurring in pneumonia, typhoid fever, and other acute infectious diseases. Within the last twenty-five years some physicians have preferred to use caffeine and other drugs when confronted with these symptoms. His communication discusses briefly the question whether failure of either the heart or vaso-motor apparatus is the chief cause of death in the infectious

diseases. He quotes various observations regarding the effect of acute infectious diseases upon the myocardium and the vasomotor apparatus. He sums up the results of these observations by stating: (1) that since there is no evidence that the vaso-motor apparatus is injured in the acute infectious diseases it is not logical to direct treatment chiefly toward this apparatus and (2) that the hypothesis that the heart may be fatally injured in the acute infections, although far from proved, is still tenable in the present state of our knowledge, and that it is consequently logical to attempt to assist it when it seems to be failing. Newburgh investigated strychnin and caffein with regard to their value as cardiovascular stimulants. He concludes that strychnin sulphate, in medicinal doses, does not increase the output from the heart, slow the pulse, or materially raise the blood-pressure, therefore there is no logical basis for its use as a cardiovascular stimulant. Caffein-sodio-salicylate, in the doses employed, does not raise the blood-pressure or slow the pulse. Newburgh points out that his observations do not permit him to state directly whether strychnin and caffein increase the efficiency of the circulation. The fact that the pulse is not slowed by any given drug does not necessarily mean that the drug may not be improving the circulation in other ways. It is equally true that rises of blood-pressure do not necessarily signify better circulation and that an increased flow of blood may occur in the absence of any marked change in blood-pressure.

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**Report of Thirty-four Cases of Artificial Pneumothorax.**—MALL (*Jour. Am. Med. Assn.*, 1915, lxiv, 897) says that the most favorable cases for lung compression are those in which cavity formation has not occurred but which, under usual methods of treatment, are progressing toward softening. In some advanced cases with large cavities, much relief of distressing symptoms may be obtained by compressing the more advanced lung. Removal of fluid with temporary compression by nitrogen gas or air is the most rapid and effective method of treating large pleuritic effusions. Hemorrhage is usually promptly and permanently relieved by artificial pneumothorax. Compression of one lung does not induce increased activity of the disease on the opposite side.

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**The Treatment of Typhoid with Non-sensitized Vaccine.**—CSERNEL and MARRON (*Wien. klin. Wochenschr.*, 1915, xxviii, 229) report encouraging results in treating typhoid fever by intravenous injections of a non-sensitized polyvalent vaccine. The details of the preparation of the vaccine are given in the article. The vaccine was so prepared that each cubic centimeter contained 15,000,000 bacilli and intravenous injections of from 1 to 2 c.c. of the vaccine were given. The intravenous injections were followed in one to one and a half hours by a chill with a decided rise of temperature which soon fell by crisis, the fall being accompanied by profuse perspiration. They believe that this form of treatment is contra-indicated in patients with severe abdominal complications, such as hemorrhage, perforation, cholecystitis, etc., also in patients with irregular heart action and in the markedly delirious and toxic group.

**The Preparation of Diabetic Patients for Operation.**—ADDIS (*Jour. Am. Med. Assn.*, 1915, lxiv, 1130) says that the method of preparing diabetic patients for operation by giving them a sugar and starch-free diet is not only useless but dangerous, because, while it may reduce the hyperglycemia and the amount of sugar in the urine, it greatly increases the chances of diabetic coma. When operation is not immediately necessary, and especially in those cases in which the decision as to whether or not an operation shall be performed rests largely on the question as to how much danger would be run by the patient after the operation because of his diabetic condition, it would be a great advantage to have some objective data to supplement the facts relative to this point, which can be gained by clinical observation. The quantity of sugar in the urine is no aid in this respect for the special danger to life is the failure, not of the sugar, but of the fatty acid metabolism. The coma in which diabetic patients die after operation is, often at least, accompanied by the excretion in the urine of large amounts of unoxidized fatty acids, and there is good reason for believing that the condition is due to poisoning by these acids. The estimation of the degree of impairment of the power of the body to oxidize fatty acids is therefore of prime importance in deciding whether or not operation is advisable in any particular case; but the amount of acetone bodies (fatty acids) excreted does not give a reliable indication of the degree of danger, because, although that amount may be small, the reserve power of the body to deal with these substances may be very slight, so that there may be a sudden failure under the special strain induced by operation, with the result that diabetic coma ensues. What is needed is a functional test of the fatty acid oxidizing power. Addis outlines a method which gives a clinical approximation of the total quantity of acetone bodies excreted under abrupt lowering of the carbohydrate content of the diet compared with a period immediately preceding it of moderate carbohydrate intake. The important point to determine is the rate of increase in the excretion of acetone bodies and not the absolute degree of acidosis. However, the absolute amounts as well as the relative increase must be borne in mind. A large relative increase in a patient who was excreting very little acetone bodies under moderate carbohydrate intake will not have the same significance as a similar increase when the previous elimination was high. The fear, excitement and under-nourishment of the patient which frequently accompany operation, brings about a call for the utilization of the food stored in the body. This food consists of glycogen and fat but the most readily available is glycogen, and there will be no very extensive breaking down of fat into fatty acids until the glycogen stores of the body are largely depleted. Even in cases in which the utilization of sugar is very defective, glycogen will diminish the amount of fat required in such emergencies. One aim of treatment should therefore be to bring about a storage of glycogen in the body before operation. The best means yet devised to this end is the oatmeal treatment introduced by von Noorden. The inability of the kidneys to excrete large amounts of fatty acids is a factor in the production of diabetic coma. To facilitate the excretion of the acetone bodies alkalis should be given, preferably soda bicarbonate. It is best to give the alkali in doses of from 5 to 10 grams in plenty of water before each two- or three-

hour feeding with oatmeal and if necessary one or two doses at night. The quantity of alkali required to make the urine alkaline is an indication of the amount of acetone bodies stored in the body, and this point should be considered in prognosis. Neither success in inducing a storage of glycogen in the body before operation, nor in keeping the urine alkaline is an absolute barrier against diabetic coma. They are only palliative measures. Shock is a large factor in the production of coma and Addis suggests that this factor may be obviated by the application of the principles of anoci association.

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**Technic of Proper Typhoid Vaccination.**—KIRSCHBAUM (*Wien. klin. Wchnschr.*, 1915, xxviii, 208) says that the objections to prophylactic vaccination at the present are the resulting symptoms of total pain, headache, fever and general malaise which last from twelve to thirty-six hours. In some cases these symptoms are so severe that the patient does not present himself for the subsequent injections. This objection holds good particularly in war camps as the soldiers are rendered unfit for duty for a period of several days. The author states that these reactions can be avoided by injecting a smaller initial dose and allowing an interval of two weeks between the first and second injections. The vaccine employed by Kirschbaum was prepared from several strains of typhoid bacilli and contained about 600,000,000 bacilli per cubic centimeter. The initial dose of the vaccine is 0.2 c.c., after a two weeks' interval a second dose of 0.8 to 1.0 c.c. is given and after another week the third dose of 1.0 to 1.5 c.c. is given. No reactions followed and Kirschbaum found the agglutinating power of the blood to be the same as with the methods formerly employed.

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**Vaccine Therapy of Typhoid Fever.**—FEISTMANTIL (*Wien. klin. Wchnschr.*, 1915, xxviii, 230) reports a series of 52 cases of typhoid treated by vaccine prepared from a weak strain of typhoid bacilli, according to the method of Besredka. He found that this vaccine retained its full activity for a period of a few weeks only. When given early in typhoid fever it seemed to reduce the duration of the disease markedly, and also a rise of temperature occurring during convalescence could be reduced by the administration of the proper dose of the vaccine. He found no evidence of this vaccine aborting typhoid as is alleged for the serum of Ishikawa. In 10 of the 52 cases various complications developed. Only one patient died, but sixteen patients are still under treatment.

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**Vaccine Treatment of Typhoid.**—EGGERTH (*Wien. klin. Wchnschr.*, 1915, xxviii, 209) reports a series of 48 cases of typhoid fever in which typhoid vaccine prepared according to the method of Besredka was injected into the brachial vein. It was given in doses of 0.5 to 1 c.c. Of 48 patients, 38 were cured, 8 showed no effect and 2 died. The injections were followed by an almost immediate rise in the temperature, from one to one and a half degrees, which lasted from six to ten hours. At the end of this time the temperature fell by crisis, accompanied in many cases by profuse perspiration. Symptoms of collapse were never noted, and there was a decided improvement in the cerebral symptoms, such as headache, dizziness, etc. The best results were obtained in

those cases which came under treatment during the first two weeks and which showed no complications. Of the two fatal cases death occurred within three hours after the injection, and Eggerth says that the autopsies showed sufficient cause to account for these deaths without attributing it directly to the vaccine.

**The Treatment of Intestinal Amebiasis.**—JONES (*Jour. Am. Med. Assn.*, 1915, lxiv, 982) says that amebiasis may exist in a mild or even advanced form without dysentery, and dysentery may persist for months or years after amebic ulceration without amebiasis. He is convinced that emetin hydrochlorid, while a valuable amebicide, if used alone will not cure amebic dysentery and that relapses will soon occur. The same statement is equally true of ipecac used alone. After an experience with each of these drugs used alone he has reached the conclusion that emetin given by hypodermic, accompanied or followed by the use of ipecacuanha by mouth, will cure most cases of intestinal amebiasis. He believes that emetin hydrochlorid is amebicidal to those entamebas which are in contact with the blood stream, that is, those deep in the ulceration, but would have little effect on those in the intestinal canal or the edges of the ulcerations. The reverse is true of ipecac, the drug given by mouth (by its emetin content) destroying the entamebas in the intestinal canal or outer margins of the ulcerations but not penetrating deeply into the irregular excavations. Ipecac has the disadvantage of producing nausea and vomiting and it has been Jones' experience that emetin hydrochlorid after several administrations produces a tolerance to ipecac which markedly lessens or prevents the disagreeable effects of ipecacuanha. He advises giving emetin hydrochlorid in doses of 0.008 gram by hypodermic for ten days (twice a day for four days and once a day for six days). Ipecac can be started about the eighth day with from 1.5 to 2 gram doses given at bedtime, continued for three consecutive nights and thereafter decreased by 0.3 gram each consecutive night. The disagreeable effects of the ipecacuanha were never manifested. It is necessary to precede the administration of ipecacuanha by tinctura opii in from 0.6 to 1 gram doses. The fact should not be overlooked that emetin is an amebicide and has little to do with the healing of ulcerations. Every case of amebiasis should, after this treatment, be considered one of ulcerative colitis and so treated from a dietetic point of view. At the same time every effort should be made to enhance resistance by change of climate, tonics, etc., to obviate the distressing sequelae characteristic of the disease.

**The Treatment of Pernicious Anemia with Salvarsan and Neosalvarsan.** BRAMWELL (*Brit. Med. Jour.*, 1915, 2827, 406) presents a further report of 21 cases of pernicious anemia treated by intramuscular injections of small doses of salvarsan and neosalvarsan. He compares his former results obtained by oral administration of arsenic and believes that he has obtained more distinct results by the use of salvarsan and neosalvarsan given intramuscularly. Bramwell says that benefit is more quickly obtained and that the duration of the improvement is generally longer and the proportion of apparent cures seems greater than where arsenic is given by mouth. He prefers the intramuscular



method of giving salvarsan in pernicious anemia, because he believes that intramuscular injections produce a sustained and continued action as opposed to a more temporary effect when salvarsan is given intravenously. Bramwell believes that salvarsan is more effective than neosalvarsan, but salvarsan given intramuscularly usually produces some febrile reaction and more or less pain at the site of injection. The intramuscular use of salvarsan and neosalvarsan have little tendency to give rise to symptoms of arsenical poisoning, especially peripheral neuritis, which sometimes develops under the continued use of arsenic by mouth. Bramwell says that his patients have not been observed long enough to make any definite statement in regard to ultimate results, but the immediate beneficial results, however, in some of the cases, were very striking.

## PEDIATRICS

UNDER THE CHARGE OF

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**Disturbances of Digestion in Infancy.**—JOHN LOVETT MORSE (*New York State Jour. of Med.*, 1916, xvi, 54) classifies the diseases of the gastro-enteric tract into nervous disturbances of the digestive tract, disturbances of digestion and infections. The first condition is caused by irritable or exhausted nerve centres causing vomiting and diarrhea. The second condition may be caused by an excess either in one food element or in the bulk of food, or by diseases or extraneous conditions diminishing the digestive powers. Indigestion with fermentation may develop from disturbances of the normal process of digestion or primarily from excessive bacteria introduced into the intestine. There are marked pathological lesions in this condition as there are in infectious diarrhea. In indigestion caused by too much or too rich a food, the amount or strength of the food should be cut down to a point lower than the normal baby of that age would be taking, and then raised carefully to the point of tolerance again when the disturbance has disappeared. The point of tolerance is best determined by examination of the stools. When individual food elements are cut down the other elements must carefully be raised to keep up the caloric value. In the case of sugar another sugar may be substituted. In protein excess regulation of the mother's life, or in the bottle-fed cases, diminishing the casein percentage, boiling the milk, addition of alkalies or citrate of sodium and pancreatization may be employed. Drugs are of little or no use in simple indigestion. Cleaning out the bowel with castor oil and by the use of enemata is an important part of the treatment. Indigestion with fermentation may be caused by the butyric acid bacilli, the colon bacillus, and even the normal lactic acid forming

organisms. It is more serious than simple indigestion, more often acute and accompanied by fever. Vomiting is uncommon while diarrhea is marked. Usually the carbohydrates and less often the fats are acted on, causing the fermentation. Lactic acid bacilli are indicated in treatment where the carbohydrates are selected by the attacking organisms, and may be given in broth cultures or in modified milk ripened by them. They are also indicted in the proteolytic type of condition. In the carbohydrate type this element should be cut down and *vice versa*. Symptoms indicating a possible fatal outcome are excessive vomiting, hyperpyrexia, irritation of the central nervous system and collapse.

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**Influences of Syphilis on the Chances of Progeny.**—M. BISHOP HORMAN (*British Med. Jour.*, 1916, No. 2875, p. 196) in investigating the causes of blindness in 1100 children also collected the family history in 150 families. In all of these families one or more children were undoubted sufferers from congenital or inherited syphilis. Besides the state of blindness there were other indubitable signs of syphilis in Hutchinsonian teeth, characteristic physiognomy, scars, bone and joint disease, deafness, etc. Whatever the evidential value of blood tests for syphilis there is certainty in this evidence presented by the finding of these other clinical features. Hutchinsonian teeth alone give certainty and association of this form of teeth with one or more of these other clinical characters provides a superabundance of certainty. In the 150 families above referred to, 68.5 per cent. Hutchinsonian teeth were present in the blind child of the family. Where evidence of the teeth was lacking there were the other symptoms in sufficient number to explain the blindness. Compared to the 150 syphilitic families a second series of 150 families were studied in which the women were not syphilitics or the progenitors of syphilitic children. The results of fertilization of these two series of women show that 150 syphilitic mothers had 1001 pregnancies, but of these only 390 resulted in healthy children, while the 150 healthy mothers had 826 pregnancies which resulted in 654 healthy children. There were 92 miscarriages per 1000 among the syphilitic series against 73 among the healthy, and 80 stillbirths per 1000 among the syphilitic against 20.5 per cent. among the healthy women. These figures speak sufficiently of the influence of parental syphilis on the chances of healthy progeny.

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**A New Treatment for Pertussis.**—RUDOLF KRAUS (*Wien. klin. Wchenschr.*, 1915, xxviii, 1405) has attempted a new principle in the therapy of infectious diseases which rests on the idea that the reactions from bacterins, etc., are caused, not by the bacteria themselves but by albuminoid bodies. He has already shown that a watery extract from agar cultures of bacteria coli gives the same results in puerperal infection or typhus as does the bacterium itself. The application of the new idea was made on pertussis. The Bordet-Gengou bacillus has been claimed by many observers to be the true cause of pertussis and been used for serum and bacterin therapy in the treatment of the disease. The results have not always been encouraging and with the idea of the efficacy of albuminoid bodies in mind Kraus utilized the sputum of children with pertussis for therapeutic purposes. The sputum of the

early paroxysmal stage was collected in sterile dishes, washed, tested for tubercle bacilli, mixed with ether, and shaken for one day to eliminate the possible spirochetes of syphilis. The ether was evaporated at  $37^{\circ}$  C. and the liquid tested for sterility, aerobic and anaerobic, and by injection into animals. The sterile fluid was then injected subcutaneously, from 0.5 c.c. to 2 c.c. every third or fourth day. No local reaction was observed. The experiments were carried on by different observers in three separate hospitals and 50 children from a few weeks to fourteen years of age, all suffering from typical pertussis in various stages, were treated in this manner. The results showed that almost invariably improvement began after the second injection, the paroxysm rapidly diminished in number and became more catarrhal in character, the vomiting disappeared rapidly in all cases and where hemorrhages were common they rapidly disappeared. In general the result was a marked improvement. The chronic cases of two or three months' standing were equally improved by this treatment as were those cases complicated by bronchopneumonia and measles. No other form of treatment previously used showed such a degree or rapidity of improvement.

## OBSTETRICS

UNDER THE CHARGE OF

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**The Prevention and Treatment of Perforation of the Uterus Complicating Abortion.**—SCHWEITZER (*Monatschr. f. Geburtsh. u. Gynäk.*, 1914, xlii) reports from Zweifel's Clinic in Leipzig 8 cases of perforation of the uterus complicating abortion. He has collected 105 in the literature with a mortality of 25 per cent. Where such patients received no treatment, the mortality rises to 50 per cent. The question as to whether the uterus in abortion is especially vulnerable has occasioned much discussion. It has been abundantly proved that there is a change in the uterine muscle in early pregnancy, so that an instrument can be inserted more readily than normal, and it is often observed that stitches do not hold and that tenaculum forceps tear out. A series of cases has been reported where pathological conditions of the uterine muscle have been found after perforation of the uterus complicating abortion. Thus a blighted ovum or molar tumor weakens the wall of the uterus through the overgrowth and penetration of the villi of the chorion. When one comes to consider how this accident can be avoided, solution of the problem is not so simple. Free manipulation upon the pregnant or puerperal uterus should be made as gently and carefully as possible. In all cases where the uterus is strongly bent, perforation may readily occur during curetting or packings. Where this accident happens in hospitals, and in the hands of good operators, it is very seldom followed by bad results. The important point seems

not to be the instrument used, but whether or no the instrument employed has been correctly used. The finger of the obstetrician may produce this lesion. So laminaria tents when introduced or when withdrawn may perforate the uterus. The effort to pack the uterus after removing the tent, which has weakened the wall of the organ, may result in rupturing the uterine wall and infecting the surrounding tissue. Where a tent disappears into the uterine cavity, it would be better to incise the uterine wall to remove it than to run the risk of injury by unskilful manipulation. So Hagar's dilators, although ordinarily a safe instrument, have repeatedly caused laceration and perforation. Very often the point of perforation is just above the internal os, so that the greater part of the uterine cavity is not in communication with the cavity of the pelvis. Cases where Hagar's dilator causes the accident seem to be especially prone to the development of infection. The most dangerous instruments, however, are those used to remove portions of the ovum. Often the fact that the cervix is not properly dilated predisposes to this accident. In endeavoring to insert the placental forceps in a narrow cervix, the tissues suddenly yield and the instrument is forced through the wall of the uterus. Especially is this liable to happen where there is a sharp flexion. Small, sharp curettes are especially dangerous. It seems possible at times to remove the small ovum with a curette, but at four or five months this cannot be done. The effort to do so will inevitably result in injury. Even in the early months of gestation the curette cannot be relied upon to empty the uterus, and the womb in these cases should always be explored with the finger. The effort to do curetting without exposing the patient and without placing her on a suitable bed or table, cannot be too strongly condemned. As complications, perforations of the intestine or wound of the intestine are especially dangerous. This, in 48 such cases, 13 died (a mortality of 27 per cent.). The injury was 25 times in the duodenum, 16 in the sigmoid flexure, 6 in the ascending and transverse colon, and in 2 in the appendix. Simple prolapse in the intestine through the rent in the uterus is not necessarily of great importance, provided it is promptly detected and the intestine replaced. Prolapse of the omentum is not of especial importance. In 2 cases the tube and ovary were injured; in 1 the urinary bladder; in 1 the right ureter and pelvis of the kidney, so that the kidney had to be removed. The patient fortunately recovered. In 1 case the promontory of the sacrum was injured by violent and unskilful manipulation. When there is a history of interference and manipulation within the uterus in a case of abortion, the case must be considered as at least a suspect from the standpoint of infection. In preventing this accident, one must take especial care to thoroughly dilate the cervix before attempting any intrauterine manipulation. A thorough examination under ether before proceeding to dilatation is indicated. In the first pregnancy the writer prefers the laminaria tent, replaced and gradually increased in size until the finger can explore the entire cavity of the uterus. A packing of iodoform gauze, to remain not longer than twelve hours, is indicated. After the fourth month he would employ Tarnier's dilating bag, although prior to that time he would carefully avoid the use of the bag. To empty the uterus he would employ the finger only. If perforation is diagnosticated, further manipulation must immediately

cease, though douching of the uterus is permissible, and some cases can be successfully treated by an ice-bag, the giving of opium and an intra-uterine pack of iodoform gauze. In 17 cases of perforation of the uterus complicating abortion, 9 died; 6 of peritonitis. One died of general sepsis, 1 of ileus, 1 of pelvic abscess, 1 had peritonitis but recovered, 1 had abscess in the pelvis, which became encapsulated and three weeks later burst into the peritoneal cavity. In 4 cases there developed a fistula between the uterus and the intestine. Of these 4, 1 died of cachexia and 3 recovered. One patient died in collapse. But 2 cases in 17 treated expectantly without operation recovered without serious complication. The mortality of cases of perforation of the uterus complicating abortion, treated without operation, is 53 per cent. These results indicate that operation should be the rule. Section should be done, and Ringer's solution should be employed to cleanse the peritoneum. If the uterus is but little injured and there is no evidence of infection, the wound in the uterus may be closed by suturing and the abdomen closed with a pelvic drain for a short time. The effort to make the operation extraperitoneal, has frequently resulted in the formation of abscess in the abdominal wall. In cases where infection is feared, radical treatment naturally consists in the removal of the uterus. In 45 cases treated by section and extirpation of the uterus, there were 9 deaths, 6 of which were from peritonitis. Of the remainder, 1 was from collapse, 1 hemorrhage, and 1 from an unknown cause. The deaths from peritonitis in those treated conservatively showed the mortality-rate of 11 per cent. while of those treated radically by operation, the mortality for peritonitis was but 2.8 per cent. There is danger in performing a superficial amputation and dropping the stump, and in 8 of these cases, 2 died of peritonitis. These were treated by vaginal extirpation of the uterus with one death from peritonitis. The presence of injury to the intestine increases the mortality 7 per cent. Of 24 treated by total abdominal extirpation, there was one death by peritonitis—4.2 per cent. The evidence seems to point clearly to the value of operative treatment, and that in the majority of cases this must be radical and not conservative.

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**The Abderdalden Test.**—As experience increases with the Abderdalden test, it becomes evident that it cannot be considered as proof positive of pregnancy, but that numerous other conditions may produce it. ABELER and LÖHNBERG (*Berl. klin. Wochenschr.*, 1915, No. 13), have tested this method with the extracts made from carcinomatous tissue and from connective tissue of the kidneys. Their series of experiments numbered 160. In none of them did they use for normal serum material obtained from the placenta. In 11 cases of extra-uterine pregnancy, 6 gave a positive, 5 a negative reaction to ninhydrin. With other observers they found that in some cases a simple hematoma of the pelvis would give a positive reaction, while in others an inflammatory tumor of the adnexa would give a positive reaction to placental extracts. In 39 cases of normal pregnancy, the method was positive in but 1 and this patient had some grave disturbance in metabolism. Among patients who were not pregnant but suffering from some pelvic disease, positive results were obtained in 19.6 per cent. Patients who had fever or tumors gave a positive reaction to placental tissue. In

the carcinoma material 82 per cent. gave a positive reaction. In general the observers believe that the Abderhalden test gives an equally good result in both pregnancy and carcinomatous disease, but to distinguish between these, has not yet been clearly determined. KEITLER and LINDER (*Wien. klin. Wchnschr.*, 1915, No. 21) in 24 cases examined, in 19 used serum obtained from placental substance only. One case gave a negative result where a carcinoma was present and others gave positive results when nitrogenous material, placental or carcinomatous, was present. In 21 cases of pregnancy the case behaved in a characteristic manner in 11. In 27 cases of carcinoma the result was clear in 15. In 21 cases of myomatous tumor, the specific reaction was obtained in 11. In these, as a substratum, the middle muscular layer of myofibromatous tumor was employed. In a series of observations made, the results of the test were far from ideal. Frequently the fault lay in some failure to carry out completely the necessary technic.

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**Criminal Abortions.**—BENTHIN (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvii, 3) has studied the frequency and results of criminal abortion from the material in Vinter's Clinic in Königsberg. He finds that at least from 19 to 22 per cent. of all abortions are criminal. All classes of society are embraced among these and the mortality from septic infection far exceeds that of ordinary parturition. The morbidity in these cases is very great and the patient's general health and ability to bear children subsequently and her power for work are very greatly damaged. These cases seem to occur about equally among the married and unmarried. Regarding the means of preventing these occurrences, Benthin warns against the prescription by physicians of vaginal douches taken by patients at their houses and also against the use of intra-uterine pessaries. Indirectly, whatever can be done to regulate and improve the guild of midwives and stamp out the work of those unreliable and disposed to do criminal operations, will also help greatly. Private maternity hospitals should be carefully supervised and all objectionable establishments should be permanently closed. All cases of abortion followed by fever should be immediately reported to the health authorities.

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**The Mortality from Puerperal Sepsis Since the Year 1900.**—BUES (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvii, 3) gives the results of his investigations on this subject from von Herff's Clinic at Basel. He concludes an extensive study of this subject by giving the statistics from twenty cities and countries, including Sweden, Italy, Germany, Norway, England, Switzerland, Austria, Paris, Berlin. The lowest mortality rate is that of the city of Basel, which he states at 0.47 per cent.; the highest that of Berlin, 5.44 per cent. England has 1.51 per cent.; Paris, 4.30 per cent.; Madrid, 3.42 per cent.; Vienna, 3.28. In recent years there has been a diminution varying from 0.01 per cent. to 0.87 per cent. in various cities and countries quoted. von Herff adds to the preceding the mortality in puerperal sepsis in Basel Clinic in 16,999 women from 1902 to 1913. In 84.76 per cent. there was absolutely no fever during nor after parturition. In 15.24 per cent. the temperature rose above 101°. The mortality was 0.58 per cent.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Practical Points in the Technic of Pyelography.**—A few minor, but exceedingly practical points for eliminating as far as possible all dangers from the performance of pyelography have recently been brought out in a short paper by WOODRUFF (*Surg., Gyn., and Obst.*, 1916, xxii, 241). The author's main plea is for *care* and *gentleness* throughout. He emphasizes very strongly that the entire cystoscopy should be carried out *directly under the x-ray tube*; "this," he says, "is the most important point in the whole procedure, and to disregard this point causes great discomfort to the patient and possibly death. The best arrangement is to have the cystoscopic room next to the x-ray room, so that wires and a window may be cut through and a tube used at any time in the cystoscopic room. . . . Where this arrangement is not feasible the x-ray room must be used." Woodruff believes that most of the injuries and deaths reported have been due to careless injecting and subsequent rough handling of the patient, and that after the collargol or other fluid has been injected the patient should be kept absolutely quiet until all manipulation has been done and the fluid has drained away. The bladder is emptied of all cystoscopic fluid in order to remove any pressure, and the patient is permitted to lie quietly on the table for half an hour after the picture has been taken to allow the kidney pelvis to empty itself. It is particularly to be insisted on that no pain shall be caused by the injection, as this implies overdistention of the pelvis. The fluid is allowed to run in entirely by gravity, the container being held in the hand of the operator so that it can be instantly raised or lowered as may be necessary. As soon as the fluid is seen trickling from the ureter alongside the catheter the picture should be taken and the injection stopped. In working with thorium solution, instead of collargol, Woodruff adds a small amount of methylene blue, so as to be able to detect it when it begins to flow from the ureteral orifice, as the thorium itself is colorless. (The use of thorium instead of silver salts, such as collargol, for pyelography, as suggested by Burns, was discussed in this department a few months ago.)

**Fatal Outcome of an Attempt to Form an Artificial Vagina.**—Of recent years numerous reports have appeared in the literature of operative procedures for the formation of an artificial vagina in cases where this structure is undeveloped or absent. In practically all these cases, the purpose has been merely to make possible the act of coitus, the internal organs in such patients being always of such rudimentary type as to preclude the possibility of impregnation. Practically all the methods that have been accompanied by any degree of success depend upon the utilization of some portion of the intestinal canal to

form the walls of the new vagina, since nearly if not all attempts to form a canal lined merely by skin flaps have resulted in such extensive contraction that in a short time the canal has failed to serve the purpose for which it was created. It follows, therefore, that operations for the formation of an artificial vagina involve of necessity opening the peritoneal cavity and interrupting the continuity at some point of the intestinal tract, a procedure that must of necessity be accompanied by a very decided percentage of risk to the patient. It is rather to be wondered at, then, that numbers of reports of serious or even fatal consequences of such operations are not on record; a recent report from the University Gynecological Clinic of Berne, by GUGGISBURG (*Zentralbl. f. Gynäk.*, 1915, xxxix, 827), illustrates, however, one of the serious dangers accompanying these operations. The patient, aged twenty-eight years, and engaged, was anxious to be married. There was no trace of a vagina, notwithstanding which fact, the patient had contracted a severe urethral gonorrhea. After this was completely healed, an operation of the typical Baldwin type was undertaken for the purpose of establishing an artificial canal. After a fossa about 10 cm. deep had been established by blunt dissection between bladder and rectum, the abdomen was opened, and a loop of intestine about 35 cm. long isolated from the ileum, continuity of the intestine being established by lateral anastomosis. This anastomosis was about 20 cm. from the ileocecal valve. Both ends of the isolated loop were closed, and the middle of the loop drawn down into the tract previously formed between bladder and rectum. The wall of the intestinal loop was then stitched to the vulvar orifice, and the intestine opened. The patient did well for three days, but then began to show signs of peritonitis, and died on the sixth day. Autopsy showed a diffuse peritonitis with complete gangrene of the isolated segment of intestine, evidently the result of constriction of the mesentery at the point where it passed through the peritoneum of Douglas's pouch.

**Autotransplantation of the Corpus Luteum.**—The question of ovarian transplantation has occupied of recent years a position of considerable interest among gynecologists, and has been discussed at various times in these pages. In most of the reported cases, the attempt has been made to retransplant into some portion of the body ovarian tissue obtained from the patient herself in cases where it was not thought advisable to leave either ovary *in situ*, because of inflammation or other pathological conditions, the purpose of this being to prevent the nervous phenomena which often accompany the artificial menopause. A report of two experiments along a somewhat different line have recently been reported by DE LEE (*Surg., Gyn. and Obst.*, 1916, xxii, 80); while both resulted in failure their distinctly novel character makes them worthy of passing notice. In both instances the patients were women in the second month of pregnancy, who were operated upon for large unilateral ovarian cysts, the corpus luteum of the pregnancy being located in the cystic ovary in such a position that it was impossible to avoid removing it. In view of the well-known theory of Fränkel and others that the continuation of pregnancy, at least in the early weeks, is dependent upon the persistence of the corpus luteum, De Lee made an exceedingly ingenious attempt in both cases to preserve the



pregnancy by excising the corpus luteum from the extirpated cystic ovary and reimplanting it between the layers of the broad ligament. One patient went for four weeks following operation, and then had an abortion accompanied by sudden relaxation of the uterus and very alarming hemorrhage, from which she eventually recovered; the other patient aborted on the twelfth day, accompanied also by rather severe hemorrhage. It would seem probable, as far as one can judge from these two cases, that the transplanted corpus luteum had been rapidly absorbed, and had been of no functional benefit to the patient.

**Unusual Case of Vicarious Menstruation.**—A remarkable and exceedingly interesting case of vicarious, or as the author prefers to term it, "compensatory" menstruation, is reported by CONDIT (*Amer. Jour. Obst.*, 1916, lxxiii, 238). The patient was subjected to a hysterectomy with complete removal (supposedly) of both tubes and ovaries for extensive pelvic inflammation consequent upon a criminal abortion performed two years previously. Two weeks after the operation (the patient's regular time for menstruation) she had all the menstrual menses, accompanied by a hemorrhage into a small nevus situated over the left ninth intercostal space. Originally the size of a split pea, in a few days the nevus was as large as a hen's egg, with considerable ecchymosis in the surrounding skin. There was no exudation of blood, however, and the tumor rapidly diminished to half its former size. This phenomenon was repeated regularly for twenty-one months, each hemorrhage causing an additional amount of infiltration, until a tumor as large as a child's head had developed, presenting a strong resemblance to a mammary gland. Eventually the tumor ruptured during one of the menstrual periods, accompanied by an alarming venous hemorrhage. It was excised, and was found to consist of dilated bloodvessels, many of which were ruptured, with extravasation of their contents into the surrounding tissue. At the time of the next following regular period the patient's left breast began swelling until it reached twice its normal size, the skin becoming ecchymotic, and the entire organ presenting a bluish-black appearance. The repeated attacks upon this breast became exceedingly alarming, and were attended with severe pain in the mamma and axilla. The gland always subsided almost to normal between the periods, and there was never any discharge of blood or other secretion from the nipple. After about a year the attacks became less severe, and by the end of two years had ceased altogether so far as the breast was concerned. Some time later, however, the patient was seized with extensive subcutaneous hemorrhages into the extensor surfaces of both legs, accompanied by pain and extreme ecchymosis from the inguinal region to the knees. These attacks occurred at irregular intervals for several months, the last occurring in July, 1914, seven years and three months after the hysterectomy. The author considers this remarkable case due to a struggle on the part of the physiological organism to compensate for the loss of the uterus, the stimulus being provided by secretion from a small portion of an ovary left at operation or from a supernumerary ovary. He considers increased vascular tension, and disintegration of blood elements important factors, and that the various vascular areas were attacked in the order of their least resistance.

## HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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**Rat-bite Fever.**—Rat-bite fever is a paroxysmal febrile disease of the relapsing type following the bite of a rat. It is due to the *Streptothrix muris ratti*, first described by Schottmüller in 1914. The wound heals readily but after a variable incubation period of a few days to a month the wound becomes inflamed and painful. Lymphangitis and adenitis set in and are quickly followed by symptoms of systemic infection ushered in by a chill and rapid rise in temperature. A characteristic exanthem of bluish-red, erythematous, sharply margined macules appears, generally distributed. About 10 per cent. of the cases terminate fatally, usually during the first febrile period, occasionally later from nephritis or exhaustion. BLAKE (*Jour. Exper. Med.*, 1916, xxiii, 39) reports the isolation of a streptothrix from the blood during life and at autopsy in a case of rat-bite fever. The organism is a true branching, filamentous organism, showing fragmentation of the myocelial filaments, granule formation, and the development of chains of coccus-like forms. It is Gram negative and not acid-fast. It is a facultative anærobe, non-motile, non-chromogenic, without capsule or spore formation. It grows in discrete colonies on Loeffler's blood serum, blood agar, and ascitic agar, and as a flocculent sediment in ascitic bouillon. No growth occurs on other media. It is only slightly pathogenic for rabbits and white rats, producing in some cases a local inflammatory and proliferative reaction at the site of inoculation and general lymph node hyperplasia. The organism is identical with a streptothrix isolated from a case of rat-bite fever reported by Schottmüller in 1914 and designated by him *Streptothrix muris ratti*. The organism was agglutinated by the patient's serum in dilution as high as 1 to 320, a fact which further substantiates its etiological relationship to the infection in this case. Pathological examination showed an acute ulcerative endocarditis of the mitral valve with masses of streptothrices in the vegetations, and infarcts of the spleen and kidney. There were subacute lesions of the myocardium, liver, adrenal, and kidneys all of a similar nature, consisting of areas infiltrated with polymuclear leukocytes, lymphocytes, plasma, and endothelial cells with varying degrees of degeneration of the normal cells of the affected area. From the results obtained in the study of his case, Blake concludes that rat-bite fever is a specific infectious disease caused by *Streptothrix muris ratti*; that the organism invades the

blood stream; that the host develops a protective mechanism against the streptothrix as shown by the presence of agglutinins; and that pathological changes of an inflammatory nature occur in the heart, kidneys, liver, and adrenals.

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**The Control of Cholera.**—McLAUGHLIN (*Am. Jour. Trop. Dis. and Prevent. Med.*, 1916, iii, 392) points out the modern method for the control of Asiatic cholera on international trade routes. Instead of the ordinary period of detention of five days in quarantine, persons may be released upon a negative stools examination. This method was made official upon the recommendation of Dr. McLaughlin by a government regulation, promulgated July 19, 1911. The importance of carriers in cholera is emphasized and the following method recommended for their detection: Specimens are best obtained by administering a saline or by using a rectal tube with "eyes" cut into it. The specimen is then planted in peptone, incubated at 25° to 30° C. for six hours, and examined not later than eight hours. A smear is made from the surface of the peptone growth, avoiding any pellicle. The smear is dried slowly and fixed with heat, stained with carbol-fuchsin, and diluted 1 to 9. It is then examined for curved or vibrio forms. All positive or suspicious specimens are plated on ordinary nutrient agar (2 to 3 per cent.) neutral to phenolphthalein, the surface of which has been dried by an hour in the thermostat. These plates are examined after about sixteen hours. Suspicious colonies are fished and mixed with specific cholera serum, 1 to 600, which should agglutinate true cholera at once. The colony is also transplant upon an agar slant for further study.

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**The Trend of American Vitality.**—Statistical studies plainly indicate that during the past ten years in the United States there has been a decrease in mortality in age groups under forty, and it is clear that this decrease has largely been due to improvement in infant mortality and control of the communicable diseases, especially typhoid fever and tuberculosis. On the other hand there has been an increase in the mortality above forty years. This increase is due to an increase in the incidence of the so-called degenerative diseases. Thus from 1900 to 1910 cancer increased 30.6 per cent.; diabetes, 60 per cent.; cerebral hemorrhage and apoplexy, 18.8 per cent.; organic diseases of the heart, 39.3 per cent.; diseases of the arteries, 396.2 per cent.; cirrhosis of the liver, 14.3 per cent.; Bright's disease, 18.1 per cent.; making an average increase of 33.8 per cent. Many reasons are given for this shortening of the expectation of life in America after forty years, but a large factor, as pointed out by DUBLIN (*Popular Science Monthly*, April, 1915), is due to the change in the "population constitution" resulting from immigration from southern and eastern Europe. Statistical studies show that foreign-born as well as the native-born of foreign parentage at the higher age periods and for both sexes have a mortality largely in excess of the native-born of native parentage. The statistics of the degenerative diseases indicate, furthermore, that the nativity factor plays an important part in determining the death rates from these diseases. Thus, both in the registration states and cities where this subject has been studied, it has been found that the native-born of

native parentage show almost uniformly a lower incidence from Bright's disease, diabetes and cirrhosis of the liver than do the foreign-born and their children. The rates, to be sure, vary considerably with the different nationalities; but, taken as a group, the foreign-born apparently show a lower resistance to the degenerative processes which these diseases imply. It is, therefore, not to be wondered at that the death rate in the large cities and States in the registration area shows an increase in mortality in the higher age groups.

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**Permanent Sediment Records for Water and Sewage.**—WHIPPLE and BUNKER (*Amer. Jour. Public Health*, October, 1915, vol. v, No. 10) report a simple method of obtaining a graphic record of the dirt in a water is afforded by the use of some device for straining a given sample through a disk of cotton batting. The sediment retained on the fibers imparts to them a discoloration in proportion to the dirt in the sample. The disk may be dried and preserved by mounting and keeping away from strong light. Any device for accomplishing the filtration is suitable, but the Wizard Sediment Tester for Milk is recommended for ease and manipulation and the uniformity in appearance of its pressed-out cotton disks. For the sake of uniformity the writers recommend the following quantities for filtration as a tentative standard: Filtered water, 1 gallon; ground water, 1 gallon; "clean" surface water, 1 quart; "dirty" surface water, 1 quart; sewage and effluents,  $\frac{1}{2}$  pint. This form of record has the following advantages: (1) It can be made easily and quickly; (2) it can be made by any one, laborer or expert; (3) it is inexpensive; (4) the records are self-explanatory and easily understood; (5) within limits, the records are quantitative and may be used for bases of comparison; (6) the records are permanent and may be mounted for preservation and photographed for reduplication. This form of record is recommended as an important addition to routine water analysis records.

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**The Destruction of Fly Larvæ in Horse Manure.**—The United States Department of Agriculture (*Bull. U. S. Dept. Agriculture*, No. 118, July 14, 1914) obtained the best results by the use of borax (sodium borate) and calcined colemanite (crude calcium borate). Both substances possess a marked larvacidal action and appear to exert no permanent injury on the bacteria. In order to kill fly eggs and maggots, apply 0.62 pound borax or 0.75 pound calcined colemanite to every 10 cu. ft. (8 bushels) of manure immediately on its removal from the barn. Apply the borax particularly around the outer edges of the pile with a flour sieve or any fine sieve and sprinkle two or three gallons of water over the borax treated mass. As the maggots congregate at the outer edges of the pile, most of the borax should be applied there. The treatment should be repeated with each addition of fresh manure. Borax may also be applied to floors and crevices in barns, markets, stables, etc., as well as to street sweepings. The borax does not appear to injure the fertilizing value of the manure. Unsatisfactory results were obtained by the use of kerosene, iron sulphate, potassium cyanid, copper sulphate, lime sulphur mixture, Paris green, sodium fluoride, formaldehyde, and the Isthmian Canal Commission larvicide.

**The Wassermann Reaction as a Clinical Test, with Special Reference to its Bearing on Matrimony.**—HEINMANN (*Jour. Amer. Med. Assn.*, 1915, lxiv, 18, 1463) calls attention to the fact that a positive Wassermann reaction may be obtained in yaws, leprosy, tuberculosis, cancer, malaria and scarlet fever, but that there could be little trouble in excluding these conditions. On the other hand, it is known that alcohol will render a positive Wassermann negative. Acidosis may excite its transitory appearance in individuals in whom it should be absent. He concludes that: The Wassermann is negative at times in active syphilis, but only under definite and characteristic circumstances, and when this is understood, no confusion should arise; the Wassermann test may be positive in the absence of syphilis, in certain other diseases, and under certain conditions easy to recognize and exclude; with these exceptions the positive Wassermann indicates active lues; clinical and experimental corroboration of this point of view exists, and thus assent to matrimony should be withheld from individuals with a positive Wassermann test.

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**The History of a Typhoid Carrier.**—W. A. SAWYER (*Jour. Amer. Med. Assn.*, 1915, lxiv, 25, 2051) reports a very interesting history of a typhoid carrier, responsible for several outbreaks. The carrier was carefully studied over a long period by officers of the Public Health Service and the sanitary authorities of California. The essential features are summed up as follows: (1) Although frequent examinations of the feces of the typhoid carrier H. O. gave negative results for four months after he had been treated with autogenous typhoid vaccine, he infected three persons when subsequently released from quarantine on parole. The total number of persons infected by this carrier, is 30, including 5 who died. (2) In a further attempt to cure this carrier, the gall-bladder and its duct were removed surgically, but the typhoid bacillus was found in the feces several times after the operation. Examination of the gall-bladder showed that it was normal and that its contents were free from typhoid bacilli. (3) After 41 successive examinations of feces during a period of fourteen months, all with negative results, the typhoid bacillus was isolated from stomach contents containing bile. (4) Certain typhoid carriers are unusually dangerous and must be controlled by quarantine or other adequate supervision.

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**Intraspinal Administration of Antitoxin in Tetanus.**—NICOLL, JR. (*Jour. Amer. Med. Assn.*, 1915, lxiv, 24, 1982) has obtained good results in treating tetanus by the following method: (1) From 3000 to 5000 units into the lumbar region of the spinal canal, preferably under an anesthetic, the volume of fluid injected being brought up to 10 or 15 c.c. by the addition of sterile normal saline, the exact amount being regulated according to the age of the patient and the amount of spinal fluid withdrawn. (2) Ten thousand units intravenously at the same time. (3) Repetition of the intraspinal dose in twenty-four hours. (4) A subcutaneous dose of 10,000 units three or four days later. The well-recognized adjuvants to specific treatment—quiet, subdued light, sedatives, etc.—were, of course, understood as a necessary part of the therapeutic measures.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Malignant Tumors of the Thyroid in the Dog.**—A considerable variation in the normal structure of the thyroid may be found in the dog. EWALD (*Ztschr. f. Krebsforsch.*, 1915, xv, 85) collected 75 cases of malignant thyroid disease in dogs to which he has added 5 cases of his own. Of these, 63 were cancers, 6 sarcomata, 7 mixed tumors and 4 were undetermined. In about half of these, metastases were found in the lung, while in only 6 were the neighboring lymph glands involved. Because of the frequency of the blood metastases he points to the greater importance of the vascular system of the thyroid as compared with the lymph channels. The secondary growths of these tumors may or may not contain colloid. This he believes is the result of tumor development from two different kinds of cells of the alveolar lining. One type produces colloid, the other does not. Normal cells passing into the blood stream do not become implanted in other organs. He does not believe that the colloid is the active secretion of the gland. The active secretion passes into the blood stream, while the colloid material, representing a useless product enters the lymph vessels. Whether the colloid and the active secretion are produced by the same types of cells is not determined.

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**Pyelonephritis.**—Three explanations have been offered upon the mode of infection of the kidney from the pelvis: (1) by the migration of bacteria upward into the tubules of the pyramids; (2) through systemic infection of the blood; and (3) by way of the perivascular lymphatics passing between the cortex and medulla. RIBBERT (*Virchows Archiv.*, 1916, cexx, 294) had an opportunity of examining various grades of pyelonephritis in soldiers with spinal cord lesions, who had developed ascending infections of the urinary system. He claims to have observed cases from the earliest pyelitis to those with marked kidney involvement. From this series he was able to follow the stages of progressive inflammation in the kidney substance. Pyelonephritis begins in an inflammation induced by bacteria or their toxins, in the interstitial tissue of the pyramids. A local leukocytosis in the capillaries and veins at the tips of the pyramids is soon followed by an infiltration in the surround-

ing tissue. The bacteria soon invade the neighboring capillaries and veins in which thrombotic masses develop. The bacterial plugs advancing in these vessels as far as the intermediate zone produce an acute inflammation along their course. In the upper portion of the medulla the bacteria pass from the infected vessels to the neighboring loops of Henle. These then become involved in a suppurative process which extends from the medulla into the cortex. Thus the purulent processes lie in streaks following the descending limb of Henle's loop. Along any portion of this route abscesses may be formed. The distribution of the infection in the kidney is confined to lobules having an infected area in the medulla. The glomeruli are not primarily affected. The author does not believe that a continuous upward infection takes place from the papilla to the cortex by way of the tubules.

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**Spontaneous Primary Tumors of the Liver in Mice.**—The occurrence of tumors in individual organs is not uniformly distributed in different species. The frequent presence of cancer of the stomach and uterus in man finds no comparison in animals. Mice commonly have cancer of the mammary gland and the lungs. Primary cancer of the liver is equally infrequent (about 0.3 per cent.) in mice as it is in man. Sarcoma is still less frequent. On the other hand, adenomata of the liver are not uncommon incidental findings in cirrhosis of the liver. Curiously enough, it has been reported that primary cancer of the liver is not uncommon in horses and dogs, while primary sarcoma has been a not uncommon primary tumor of the liver in rats. It has also been reported that these hepatic sarcomata are associated with parasitic cestodes. SLYE, HOLMES and WELLS (*Jour. Med. Research*, 1915, xxxiii, 171) found but 2 cases of tumor of the liver in mice. This appears remarkable in view of the frequency of spontaneous tumors in these animals. In a series of 10,000 autopsies on mice which had died natural deaths, they found 28 growths in the liver of the nature of adenoma. Since many of these mice were under a year old, they believed that the general incidence is considerably higher than 3 per 1000. Fourteen of the animals were males and 14 females. Cirrhosis of the liver was not present. There was no inflammatory process which might be suggested as predisposing to tumor. Of the 28 adenomas, 3 had characters of malignancy, 1 having multiple metastases in the lungs. Three others showed histological characters suggestive of malignancy, while the remaining 22 were benign. None of these tumors had characters of a bile duct new growth. Jaundice and ascites were absent. The tumors have a tendency to appear as multiple primary masses. Ten of the cases showed more than one tumor. Sarcomata were not found in any of the series.

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**The Development of Giant Cells in the Tubercle.**—There are two main theories concerning the origin of the Langhans giant cell: (1) as arising from fixed tissue cells; (2) having an origin from wandering cells, particularly from macrophages. Furthermore there is still lack

of agreement upon the manner in which the multiple nuclei appear within the giant cells. HERNHEIMER and ROTH (*Ziegler's Beiträge*, 1915, xi, 1) have again attacked the problem by an examination of human material obtained fresh at operation. They believed that from an analysis of many sections, they are able to definitely state that the epithelioid cell is directly derived from fixed tissue cells. These cells, they claim, belong to the connective-tissue group, but they do not exclude in their discussion the possibility of their endothelial nature. They had previously observed the participation of the Eupffer cells in giant-cell formation. They report a curious stellate structure within the epithelioid cells, which may also be found in the various stages of giant-cell formation. It is suggested that the asteroid bodies recently described by many (Wolbach, Vogel, and others) are the degenerated remains of abnormal centrosomes. By appropriate methods such stellate masses may be observed in many giant cells. Their studies have furthermore led them to conclude that the nuclei of the Langhans cells are developed through amitosis and not by the fusion of neighboring elements.

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**The Part Played by the Acid of the Gastric Juice in the Pathological Processes of Gastric Ulcer.**—BOLTON (*Jour. Path. and Bacteriol.*, 1915, xx, 133) believes that the most important factors in the production of ulcer are hyperacidity and motor insufficiency. Both of these factors are the most common manifestations in gastric ulcer. In the present work, he tested out the effect of each of these on monkeys and some cats. In one series of experiments he obtained a gastrototoxic serum by inoculating gastric cells into a goat. This serum when injected into the stomach wall of monkeys gave rise to hemorrhage and ulceration. Under normal conditions these ulcers healed rapidly. When, however, an artificial hyperchlorhydria was induced the ulcers were delayed in healing. Bolton also continued the experiment of serum injection and hyperchlorhydria with an experimental motor insufficiency. Under these conditions the ulcers were larger and showed less evidence of repair. This indolency of the ulcer is ascribed to hyperacidity and food retention. When hyperchlorhydria alone was present, a definite chronic inflammation of the mucous membrane was induced. A greater amount of mucus was present on the lining of the stomach and not uncommonly petechial hemorrhages were found. Sometimes these small hemorrhages were associated with follicular ulcers. The various ulcers that he was able to produce in animals were, for the most part, superficial, but sometimes extended to the muscular coat.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1913 Spruce St., Phila., Pa., U. S. A.







*Amirai Whai.*

J. WILLIAM WHITE, M.D., LL.D.

At the Quater-Centenary celebration of the University of Aberdeen, honorary degrees were conferred upon His Grace the Archbishop of Canterbury; His Serene Highness, Albert, Prince of Monaco; Becquerel, Professor of Physics in Paris; Andrew Carnegie; Krönecker, Professor of Physiology in Berne; Löffler, Professor of Hygiene in Griefswald; Lombroso, Professor of Psychiatry in Turin; Marconi, Annihilator of Space, Trendelenburg, Professor of Surgery at the University of Leipsic; upon J. William White, John Rhea Barton Professor of Surgery, University of Pennsylvania, and upon other distinguished men.

To this celebration delegates were sent from universities and educational institutions the world over. Dr. White being asked to speak for the representatives from the United States, of whom there were many, responded as follows:

"I should have had much hesitation in assuming the responsibility of speaking of American universities in the presence of so many of their distinguished representatives were it not that a very special tie connects the University of Aberdeen with my University—the University of Pennsylvania. In 1754 you sent us our first Professor of Logic and our first Provost in the person of William Smith, born within a few miles of this city, baptized 179 years ago in an old Aberdeenshire kirk, and brought up at this University. He was the grandson of Alexander Duncan of the Camperdown family and a great grandson of Colonel Peter Murray of Auchtertyre, and if there be any Murrays or Duncans or Smiths here present I beg to tender them our much belated thanks.

"I must reluctantly admit that we promptly put Provost Smith in jail for alleged seditious utterances, and in jail, with true Scottish pertinacity, he remained for two months in default of a retraction which he refused to make as the price of his freedom. But with a devotion to duty that was and is a national characteristic, he insisted on continuing his instruction to his classes, and, with what I hope I may venture to call American liberality, he was permitted to do so, and for eight weeks actually gave lectures on logic, ethics, and natural philosophy in the county prison.

"During this time, with a certain shrewdness and foresight that I have also heard described as characteristic, he wooed and won the daughter and heiress of a co-criminal, Judge Moore, and left jail with a handsome wife and a comfortable fortune. On the whole, America did not treat the first representative you sent us so very badly.

"But the debt my University owes you on account of Provost Smith—and a very good provost he made—is nothing compared with the indebtedness of all American universities to their elder sisters in Scotland. Aberdeen, Edinburgh, Glasgow, St. Andrew's were our exemplars, the source of both our plans of organization and our method of instruction, and our obligations in this way are so varied and so extensive that they can only be gratefully alluded

to in the three minutes you have parsimoniously allotted to a congratulatory speech.

"It is true, however, that the community of educational ideas and procedures thus established constitutes in conjunction with our common ancestry and our common language (if Mr. Roosevelt and Mr. Carnegie do not succeed in making the latter altogether too uncommon) a bond which tends to unite in closer and closer alliance of regard and affection the two great English-speaking peoples and thus equally tends to promote the peace and the civilization of the world.

"With universities, as with men and women, age, if time has been well spent, brings position and respectability and dignity. The representatives of America are delighted to see here on every hand evidences that it has not also brought decay or decrepitude, but rather increased strength and vigor and vitality; that they recognize with the keenest gratification that the splendid record of four centuries of educational usefulness and public service behind the University of Aberdeen promises to be equalled or even surpassed during many centuries yet to come."

This address, marked by a delicacy of appreciation, a purity of diction, and a rare touch of humor, is more characteristic of Dr. White the scholar than could be any written description.

He was in addition essentially a man of action; to many with whom he came in contact, a problem, and at times a difficult even a painful one, in eruptive dynamics.

Gifted with amazing physical strength, assiduously cultivated, with tireless activity purposefully directed, with a forceful diction which could be provoked to riot, with a fearless determination, strengthened by opposition, with loyalty to friends which recognized no limitations, with hostility toward enemies which knew no salve; his ways were direct ways, strong ways, sometimes violent ways, always honorable ways which usually attained their ends because of the clear vision and ripe judgment which marked such ends as desirable; and partly because there was no rest for himself nor any other until such ends were attained. Rest as usually understood was a thing unknown to him.

To the University in the main this vivid, forceful, active life was devoted. How purposefully need not be set forth here. In a hundred years when his diary and memoirs are published by the then Professor of Literature, Pennsylvania men of that day may have as grateful appreciation as do we, of the debt owing to White. Fortunately for them they will not have a feeling of personal loss too deep and strong for expression.

"As life runs on the road grows strange  
With faces new, and near the end  
The milestones into gravestones change;  
'Neath every one a friend."

EDWARD MARTIN, M.D.

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ORIGINAL ARTICLES

**SOME PHASES OF THE NEPHRITIS PROBLEM.<sup>1</sup>**

BY HENRY A. CHRISTIAN, M.D.,

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SOME of my predecessors as lecturers before the Harvey Society have selected topics of which it was possible to present a quite comprehensive review of contemporary knowledge within the limits of such a lecture, while others have had personal investigations to report of such completeness and importance that their presentation fulfilled amply the requirements of the occasion. My subject and my own work fall within neither of these groups. From the vast literature on nephritis no reviewer could condense into the space of an hour any adequate presentation of the results of the many valuable investigations of the past, while my own studies have not a value deserving the occupancy of an hour of your time. I have chosen to mention only certain phases of the nephritis problem illustrative of the present-day view-point of the subject and indicating the trend of recent investigation. In doing this I will speak relatively more of the work during the past eight years of myself and my associates in the laboratory of the Department of Medicine at Harvard and the Medical Clinic of the Peter Bent Brigham Hospital than of the work of others because I am more familiar with our own work, and not because I have the opinion that it is of proportionately as great value as many of the splendid researches that have come in the last decade from other laboratories and clinics.

<sup>1</sup> A lecture delivered before the Harvey Society in New York on March 11, 1916.  
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From the time of Bright's publication in 1827, with which began any real knowledge of nephritis down to the late 90's, almost all investigators concerned themselves with renal structure in nephritis or with statistical study of symptomatology. In these studies structure rather than function was predominantly the point of interest. A conception of the relations of the diseased kidney to the patient's symptoms was evolved in large part from an examination of kidneys from men dead of nephritis. Hypotheses as to the probable relations of these pathological changes to observed symptoms and to disturbances in urinary excretion were formed.

Beginning in 1900 interest shifted toward animal experimentation. Renal function in nephritis, whether produced experimentally in animals or arising naturally in men, replaced renal structure as the problem of greatest interest. A considerable proportion, however, of this interest in renal function was founded on the hope of a more satisfactory correlation of renal function as observed during life with changes in renal structure as found after death—a hope as yet unrealized, in fact, almost given up as an unattainable goal.

In 1907 I became interested in the problem of nephritis, and since then have devoted such time as was available to the study of some of these problems. In this study I have had associated with me a number of men—R. M. Smith, Walker, O'Hare, Dawson, Fitz, Frothingham, Peabody, Smillie and Woods, whose independent work I will describe in connection with my own.

We began with a few of the problems of experimental nephritis. Our first study, the work of R. M. Smith,<sup>2</sup> was on the origin of urinary casts. Two views prevailed: one that all casts originated from disintegrated tubular epithelium, the other that some of them at least were formed from albumin which escaped through the damaged glomeruli. Acute types of experimental nephritis furnished excellent material for the study of this problem, inasmuch as the urine might be examined in relation to renal lesions of varying severity and age and at any period the kidney might be studied histologically. From our work it seemed very probable that all casts were composed of material primarily coming from degenerated tubular epithelium and that granular casts were relatively young casts, hyaline casts older in the sense of requiring a longer time for their preparation. It did not seem very probable that albumin excreted from the glomerulus in solution would coagulate or precipitate in the tubule, though this mechanism might easily take place with fibrin casts if such really ever occurred in the urine.

The work of Schlayer and his co-workers at about this time had aroused much interest in the functional disturbances resulting from experimental acute renal lesions. They had differentiated the two main groups of disturbances, the tubular and the vascular, and

<sup>2</sup> Boston Med. and Surg. Jour., 1908, clviii, 696.

had outlined the functional disturbances characteristic of each. In their work they had emphasized the frequent discrepancies between functional change and demonstrable anatomical lesion, especially in the group of vascular nephritides. O'Hare and myself undertook a careful study of the finer histology of some of these experimental lesions, and were able to show that in the vascular group, glomerular lesions were more common than Schlayer and his co-workers had found, and that they occurred in a considerable variety of forms. One of these lesions consisting of the deposition of fine hyaline granules in the wall of the glomerular tuft was a type of glomerular degeneration previously undescribed,<sup>3</sup> while others of them were similar to lesions sometimes or often found in human kidneys.<sup>4</sup> Still there remained a definite discrepancy between functional disturbance and anatomical change in the kidney, and our histological studies did not throw much light on the nephritis problem in man whether looked at from a functional or from a structural view-point.

Experimental acute lesions lend themselves well to study with functional tests. It was interesting to see the relation of the phenol-sulphonephthalein test to the non-protein nitrogen or urea nitrogen of the blood; the phthalein output quickly drops, the blood nitrogen more slowly increases; the former expresses the immediate functional condition of the kidney; the latter measures the result of the past and present hinderance to renal excretion.<sup>5</sup> In the same way the amylase in the urine was studied by Fitz<sup>6</sup> in contrast to the urea nitrogen of the blood. Fitz found that amylase followed much the same curve of excretion as did phthalein, but as a test for renal function was less delicate than the phthalein test. As had been done by Schlayer, water, salt, lactose, and potassium iodide excretion were studied. Using experimental lesions, since their severity can be controlled very accurately, a good understanding of several of these functional tests and their relative values was obtained by us and by others more quickly than would have been possible from the study of human acute nephritis when much time would have been lost in waiting for the necessary number of suitable cases to turn up, and so for experimental study we were in a better position to apply these tests to human cases.

Equally well are the acute experimental lesions adapted to the study of the effect of diuretic drugs. O'Hare, Walker, Dawson and myself have investigated in this way theobromine sodium salicylate,<sup>7</sup> theocin, caffeine, potassium acetate, and water<sup>8</sup> and found

<sup>3</sup> Christian, *Boston Med. and Surg. Jour.*, 1908, clix, 8.

<sup>4</sup> Christian and O'Hare, *Jour. Med. Res.*, 1913, xxiii, 227.

<sup>5</sup> Frothingham, Fitz, Folin, and Denis, *Arch. Int. Med.*, 1913, xii, 245.

<sup>6</sup> *Arch. Int. Med.*, 1915, xv, 524.

<sup>7</sup> Christian and O'Hare, *Arch. Int. Med.*, 1913, xi, 517, and O'Hare, *Arch. Int. Med.*, 1915, xv, 1053.

<sup>8</sup> Walker and Dawson, *Arch. Int. Med.*, 1913, xii, 171.

that all tended to shorten rather than prolong the life of animals with severe acute uranium nitrate nephritis. Over short periods of time with animals anesthetized with urethane, Fitz<sup>9</sup> found that with an acute renal lesion produced with uranium nitrate, theobromine sodium salicylate and theocin caused an increased output of water, sodium chloride, and nitrogen, and did not diminish phthalein excretion; while with a lesion produced with potassium bichromate there was no increased output of nitrogen, and phthalein excretion was diminished when there was a mild renal lesion. Using phthalein as a measure of renal function we were unable to discover any definite constant improvement in renal excretion following the use of the theobromine sodium salicylate. When the lesion was severe the phthalein usually indicated that the diuretic had made the function of the kidney worse.<sup>10</sup> These diuretic substances quickly lead to renal fatigue with decreased excretion. Our experiments, as a whole, indicated harm rather than benefit from giving diuretic drugs in acute nephritis.

Very interesting observations were made on the relation of potassium excretion to renal lesions. In one of our patients with chronic nephritis it was noticed that a substitution of potassium chloride for sodium chloride in a dietary test of renal function produced toxic symptoms. In animals with acute experimental renal lesions Smilie<sup>11</sup> found that a stage was soon reached measured by a non-proteid nitrogen value in the blood of 100 mgm. per 100 c.c. of blood in which the kidney was very slightly permeable to potassium salts. Under these conditions potassium salts were markedly toxic, rapidly causing the death of the animals, though an animal with a normal renal function could tolerate large doses of potassium without any evidence of injury. The rapid excretion of potassium with an intact kidney prevented any evidence of toxicity; delay excretion by a renal lesion and toxicity at once became evident. These studies indicate that large doses of potassium iodide, for example, might be definitely injurious in a patient with markedly impaired renal function.

In man chronic rather than acute renal lesions are encountered most often, and the problems of chronic nephritis receive the greatest attention from pathologists and clinicians. Could one produce with regularity in animals various types of chronic renal lesions analogous to those found in man, many problems could be studied by methods not applicable to the human being. To produce such a chronic nephritis experimentally many efforts have been made. Like other experimenters we have been able to produce in animals, chiefly rabbits, lesions of a chronic nature with connective-tissue overgrowth very similar to those found in the types of chronic

<sup>9</sup> Arch. of Int. Med., 1914, xiii, 915.

<sup>10</sup> Christian, Arch. Int. Med., 1914, xiv, 827.

<sup>11</sup> Arch. Int. Med., 1915, xvi, 330.



nephritis seen in man. With repeated sublethal doses of uranium nitrate and of potassium bichromate, chronic experimental lesions were produced by Smith<sup>12</sup> and similar, possibly more constant, results were obtained by O'Hare<sup>13</sup> with a combination of a chemical substance (uranium nitrate) and bacteria (*B. coli communis*). These lesions were quite similar to those obtained by other observers using a variety of substances as causative agents, but all alike fail of the intent held by most workers—namely, to produce regularly chronic lesions capable of functional study with a view to throwing some light on the cause, the symptomatology, and the treatment of chronic nephritis in man. The kidney of animals possesses a surprising power of regenerative repair which makes uncertain the production of chronic lesions. Moreover, however close the resemblance, it cannot be said that in animals a condition identical with chronic nephritis in man has been produced as yet by any experimenter. Finally, the methods usually employed for the production in animals of such chronic lesions are at best only remotely related to any possible causative factors of chronic nephritis in man.

To help in any understanding of human chronic nephritis chronic lesions must be produced in animals with great regularity, and they must cause in the animal changes of a nature similar to those observed in man, such as vascular hypertension, cardiac hypertrophy, dyspnea, edema, uremia, etc., before much information can be gained about chronic nephritis from animal experimentation. Looked at in this way all work on experimental chronic nephritis falls short, though some of the phenomena mentioned above can be produced. However, it does not seem impossible that in some animals a true chronic renal lesion with the typical secondary conditions that go to make up the picture of chronic nephritis in man should be produced by experimental methods of investigation. Such an accomplishment would facilitate undoubtedly the unraveling of the nephritis problem in man, and its value would be so great that it is well worth while to continue to strive for its attainment.

Though the experimental studies of Schlayer and his co-workers<sup>14</sup> differentiated two very distinct types of renal lesion, the vascular and the tubular, and though with their methods of study each type was shown to cause very characteristic disturbances of renal function in animals, the value of these studies has been rather in re-arousing interest in the investigation of renal function in human nephritis than in furnishing us with any satisfactory functional classification of renal lesions in man. In each case of human nephritis both tubules and vascular apparatus usually are involved. The one structure or the other may be disturbed in greater amount, but it has not been possible, except in very few cases, to separate the

<sup>12</sup> Arch. Int. Med., 1911, viii, 481.

<sup>13</sup> Ibid., 1913, xii, 49.

<sup>14</sup> Schlayer and Hedinger, Deutsch. Arch. f. klin. Med., 1907, xc, 1.

patients with any sharpness into cases with tubular lesions and cases with vascular lesions in the sense of Schlager and his co-workers. Two of the substances which they used for functional testing in animals have hardly in the human being measured up to the usefulness which might have been anticipated from the results in animals or which was claimed at first from their use in man. Schlager utilized the time required for the excretion of a given amount of potassium iodide as an index of tubular efficiency and the time and amount of lactose excretion to indicate the efficiency of the glomeruli. We, like other observers, have used these substances in a very considerable number of patients, but gradually have discarded them as furnishing comparatively little useful information.

Widal and his co-workers<sup>15</sup> studied the renal excretion of sodium chloride and nitrogen and grouped their cases of chronic nephritis into those with deficient power to excrete sodium chloride, which cases usually showed edema as a chief symptom, and those unable to excrete nitrogen readily in which uremic manifestations generally were prominent. Our study of salt and nitrogen excretion except in an occasional case has not yielded any sharp differentiation of patients. There is an occasional patient with a marked inability to excrete sodium chloride who becomes edematous when sodium chloride intake exceeds sodium chloride output and whose kidney shows but little if any impairment of its function to rid the body of nitrogenous substances; but such cases often are not, strictly speaking, cases of nephritis but rather patients with disturbed salt elimination, and no more to be regarded as nephritis than would be cases of diabetes mellitus or diabetes insipidus. If the typical cases of chronic nephritis, whether edema is a prominent feature or not, are investigated with respect to salt and nitrogen elimination it has been our experience that in most patients both show delayed excretion; in the earlier stages salt excretion rather than nitrogen excretion is disturbed, but as the disease progresses, nitrogen excretion becomes increasingly delayed until in advanced cases both salt and nitrogen excretion are markedly and about equally disturbed.<sup>16</sup> We have not encountered cases of the type described by Widal with normal salt excretion and delayed nitrogen excretion.

In all of the earlier functional studies of patients with nephritis the desire to make an anatomical diagnosis has been prominent; sometimes it has been the acknowledged goal, at other times, though not so stated, it is evidently the aim of the investigator. Little by little it has become recognized that such an attainment has not been approached with any closeness, and I think by most investigators it is now regarded as improbable that we will ever be able to correlate closely postmortem anatomical appearance with the

<sup>15</sup> *Mouvement Méd.*, 1913, I, 1.

<sup>16</sup> Frothingham and Smillie, *Arch. Int. Med.*, 1915, xv, 201, and Frothingham, *Am. Jour. Med. Sc.*, 1915, cxlix, 808.

functional disturbances of the kidney during life, at least so long as present pathological technic and classification continue in use. Improved methods of studying renal lesions, of course, may change these conditions at any time. In a number of patients we have had the opportunity to carry out a group of functional renal studies, and on the death of the patient have submitted the kidneys to pathological examination.<sup>17</sup> In these patients there was no evident relation to be made out between anatomical changes in the kidney and antecedent functional disturbances in any selective sense that would justify an anatomical classification. In our experience in a functional sense, patients with nephritis do not separate themselves into distinctive groups; rather is it indicated that there is a progressive increase in functional disturbance with advance of the lesion, though there is an undoubted tendency for certain cases to show continuously a much more marked impairment of function as measured by one set of tests than by another, indicating that functional disturbances depend on selective excretory activity, and that were not the various renal structures pretty generally involved in nephritis a more definite classification based on tests of renal function could be made.

However, at the present time tests of renal function are of more value for indicating the presence of a renal lesion, for measuring its extent and for indicating its management than as a means of classification of cases. For these purposes they add greatly to the value of our clinical study of patients with nephritis. Out of the very numerous methods of testing renal function certain ones have survived either by reason of ease of application or by reason of yield of information in proportion to the amount of labor they require. Some have been discarded because the same information may be obtained from simpler procedures or from ones requiring less complicated and expensive apparatus or occupying less time in their carrying out. Others have been given up because they caused more discomfort and inconvenience to the patient than some other one yielding the same information. Those that are still in use, though they yield much valuable information, are not thoroughly satisfactory, and better ones probably can be worked out with our increasing knowledge of renal function under varying conditions in man and animals.

The functional tests now most generally used are the ones which show the power of the kidney to excrete a dye-stuff and those that measure the efficiency of the kidney in the excretion of water, salt, and nitrogen. Of the former group the phenolsulphonephthalein test of Geraghty and Rowntree<sup>18</sup> very largely has superseded all others as being the best of these tests, owing to its simplicity and its accuracy.

<sup>17</sup> Frothingham, *AM. JOUR. MED. SC.*, 1916, cli, 72.

<sup>18</sup> *Jour. Pharm. and Exp. Therap.*, 1910, I, 579.

To determine the excretion of water, salt, and nitrogen, several methods are employed. These substances are quantitated in the urine in relation to a fixed dietary intake; or they are quantitated in the blood; or the relation between the amount in the blood and the urine is expressed in the form of a formula of excretion.

The impetus more recently to the study of urinary water, salt, and nitrogen in relation to dietary intake we owe to the German clinics, especially to von Monakow<sup>19</sup> and to Schlayer and Hedinger.<sup>20</sup> Two general plans have been followed. By one of these the patient is on a fixed diet containing a known amount of fluid, salt, and nitrogen. By quantitating these substances in each twenty-four-hour amount of urine the promptness and completeness of excretion of the added salt and nitrogen are determined. Delay in excretion or incomplete excretion is indicative of disturbed renal function.

By another plan on one day the patient has a standard mixed diet containing definite amounts of salt, nitrogen, water, and purin bases, in certain of the meals little, in others a considerable amount. The urine is collected in two-hour portions and the salt, nitrogen, and specific gravity of each portion is determined. The curves of excretion as plotted from the values so obtained in comparison with the excretion from normal kidneys indicate departure from normal renal function.

The determination of these substances, salt and nitrogenous bodies, in the blood has been made by numerous observers in the past, but the simplified methods of Folin<sup>21</sup> and of van Slyke<sup>22</sup> recently have stimulated and made possible many new and excellent investigations of this phase of the subject.

To Ambard<sup>23</sup> is due most credit for our present interest in the rate of excretion of nitrogen and salt as determined from formulae which take into account the concentration of these substances in blood and urine, rate of urine flow, and weight of the patient. Ambard and his co-workers have worked out many of the laws governing these excretions and have shown their constancy under normal conditions. McLean,<sup>24</sup> by a slight variation in the structure of the formula of Ambard, has expressed the excretion as a numerical index which has some advantage over Ambard's way of expressing his results. Van Slyke's urease method of determining urea has rendered more accurate the determinations, and this method has been used by McLean to give a greater constancy to his figures than would have obtained with the older methods of determining the urea. However, it is only fair to Ambard and his co-workers to say that the work of others has amplified rather than corrected the conclusions drawn by Ambard from the studies made by himself and his associates.

<sup>19</sup> *Deutsch. Arch. f. klin. Med.*, 1911, cii, 218.

<sup>20</sup> *Ibid.*, 1914, cxiv, 120.

<sup>21</sup> *Jour. Biol. Chem.*, 1912, xi, 193.

<sup>22</sup> *Ibid.*, 1914, xix, 211.

<sup>23</sup> *Physiologie Normale et Pathologique des Reins*, Paris, 1914.

<sup>24</sup> *Jour. Exp. Med.*, 1915, xxii, 212.

The work of all of these observers is open to the criticism that each observer has used, as a rule, but a single method of studying renal function, usually the method devised by himself, and he has not compared often the results that might be obtained by applying to the same patients several methods of study. Furthermore, it is surprising how few of the cases studied by functional methods have had checking up from postmortem anatomical study. We have already called attention to the unsatisfactoriness of the correlation between histological changes in the kidney and prior functional renal study. Still, the autopsy checking up of results is very salutary and, of course, excludes certain errors, such as the diagnosing of a simple chronic passive congestion as a chronic nephritis. It is to be remembered, however, that most of the fatal cases will have had functional study under the handicap of the seriousness of the patient's condition hindering the carrying out of many functional studies and really represent the function of the late stages of a nephritis in relation to postmortem findings. As already stated we have had a certain number of cases for functional study and later have had opportunity to examine their kidneys. However, in almost all of these the dietary tests were impossible of carrying out satisfactorily, owing to the advanced stage of the disease, and so the studies of renal function were incomplete. It will be necessary to make studies of renal function at intervals during the course of nephritis, and then on the death of the patient study the kidney histologically before a satisfactory verdict can be rendered on the relation between renal function and renal structure, as shown by the pathological study of the terminal stage of the nephritis.

We have been able to study a considerable number of non-fatal cases with a variety of methods of testing renal function, such as the phenolsulphonephthalein test, the added urea and salt dietary test, the test renal day, the determination of the indices of urea and salt excretion, etc.<sup>25</sup> Some of these tests can be carried out almost simultaneously; others of them require several days, and only one at a time can be done. For these reasons there is the possibility for variations in the patient's condition influencing renal function, so that in comparing the results of different tests conditions are not always identical. Still in most cases there is a surprisingly close parallelism between the results obtained from different methods of testing renal function. Almost always a low phthalein output is accompanied by an increase in urea or total non-protein nitrogen in the blood, and the index of nitrogen excretion is proportionately lowered below the average normal figure. In these cases dietary tests of any sort show delayed excretion of nitrogen and salt with fixation of specific gravity and percentage concentration of nitrogen and salt. Occasionally there are exceptions

<sup>25</sup> O'Hare, paper to appear in *Archiv. of Int. Med.*

and one set of tests indicate less disturbance of renal function than another set. In some of these patients these variations are obviously due to extrarenal causes or changes in the patient's condition during the course of the testing. There remain, however, a few cases where no explanation can be found for failure of the results of different tests to agree, and for this reason alone it is important not to confine one's study of renal function to too few tests, however satisfactory the individual test would seem to be.

Patients who show these marked disturbances of renal function as measured by several tests usually are quite evidently seriously ill patients when studied merely by the regular routing methods of history of symptoms and simple physical examination. They are undoubted cases of advanced chronic nephritis, and there is no question as to diagnosis; renal tests are not needed to make the diagnosis and really do not help from that view-point. Nevertheless, by using tests of renal function some cases are found which, while showing marked disturbances of renal function, have but few if any symptoms and appear to be but slightly sick individuals. Their poor renal function comes as a great surprise to the clinician in charge. Here the tests are of much use in making a prognosis and enable the physician to warn his patient of impending catastrophe. Although he may be unable in any way to prevent this catastrophe, fore-knowledge of it may be of incalculable value to the patient and family. In our experience in such cases the progress of the disease has borne out the accuracy of the information from the tests of renal function, provided they have not been made during a period of acute exacerbation of renal disturbance or when renal insufficiency is aggravated by an increased, though temporary, circulatory insufficiency. In cases in which there is any suspicion of these conditions the renal tests should be repeated after an interval. In our experience, however, acute exacerbations of renal disturbance and circulatory deficiencies are evident in studying almost all of the cases, and should not form any appreciable source of error in interpretation. Obviously tests of renal function like all clinical tests should not be exalted into a fetish; without an admixture of brains and common sense they can lead to absurd conclusions with the man who is willing to stake all on a single test. A recent excessive ingestion of proteid by a patient with a stricture of his urethra, but otherwise healthy, could easily simulate a marked renal insufficiency by several tests and mislead that type of clinician who with but a scant glance at his patient and no conception of the patient's symptoms rushes to his laboratory tests, with the idea that scientific accuracy increases by the square of the distance from the bedside and by the cube of the time spent in carrying out a test out of touch with the sick man. This would seem so evident a proposition as not to need repetition, and yet I regret to say that I have seen almost this identical mistake made.

As I have pointed out earlier in this paper, tests of renal function have a value for three purposes: for diagnosing the presence of renal lesion, for measuring its extent, and for indicating its management. For diagnosing the presence of marked renal disturbances the tests as just pointed out are not of great value because the existence of marked nephritis is usually evident without them. In the earlier stages of nephritis tests of renal function are of considerable value in diagnosis. It must be admitted that albumin and casts in the urine are among the most delicate indicators of disturbed renal function. When found the question arises, Do they indicate a disturbed function of a type to be regarded as a nephritis that will progress? In these earlier cases phenolsulphonaphthalein excretion is so nearly normal as to be of no diagnostic aid. Non-protein nitrogenous bodies in the blood are well within normal limits and their determination does not help. It is in these earlier cases that the dietary tests indicate distinct disturbance of the type found in definite chronic nephritis, though the disturbance is less evident than in a somewhat more advanced stage of the lesion. Delay in excretion of sodium chloride, a tendency to fixation of specific gravity, hypersensitivity with polyuria or rapid fatigue, all are suggestive of an actual nephritis in the patient with slight albuminuria or cylindruria. We have found just these changes in cases in which phenolsulphonaphthalein output was good and blood urea was normal, but in which symptomatology, slight edema, moderate hypertension, etc., seemed to clearly indicate that they were cases of early chronic nephritis. Very likely without this collateral evidence a diagnosis of early chronic nephritis should be made on patients with slight albuminuria, and these changes just enumerated as indicated by dietary tests. These cases very frequently show, too, a lowered index of urea excretion and often a plus salt balance, and these methods are of equal value with the dietary tests.

We should not be too dogmatic, however, with regard to the diagnosis of early stages of chronic nephritis by renal dietary tests or determinations of the indices of urea and salt excretion. Almost all of these studies have been made very recently, and one is not justified in saying that a patient with these slight disturbances of renal function is in an early stage of nephritis until many such cases are tested and watched and retested over a period of five or ten years and found to develop with great regularity into typical cases of chronic nephritis, which means that they show themselves to have a progressing renal lesion ultimately fatal and showing at the postmortem examination an anatomically demonstrated chronic nephritis. We are in danger in present enthusiasm to overlook the fact that in the study of a chronic disease almost no method can have a proved value until much time has elapsed. Such a proved value certainly cannot be attached at present to these tests of renal function.

What are the relative values of dietary tests such as the added salt and urea test and the dietary test renal day as compared with the determination of the indices of urea and salt solution? I do not believe that we are in a position to give an answer now. As I have already pointed out in our patients all the tests agree surprisingly well, but we have not observed long enough the very early cases to be justified in holding any definite opinion as to relative value. The dietary tests are time-consuming for both patient and laboratory worker unless they can be simplified materially. Their inapplicability to ill patients unable to take the diets does not apply to early cases, but other objections do. The determination of the indices of excretion are quicker for the patient at least and simpler in not requiring hospital observation and a weighed diet. It seems to me, however, that variations in the indices in relation to variations in water output are not sufficiently well understood to justify our feeling completely satisfied with them. Then the occasional abnormally high indices that we get have not received satisfactory interpretation; they too require the time element and repetitions from period to period to be understood. So I feel that both methods of testing renal function should be persisted in for a much longer time before we are justified in giving up either one in favor of the other.

What value have these tests in prognosis? It is in this connection that we get most help from tests of renal function. The tests aid very greatly in determining the severity of renal involvement and so aid in making a prognosis. The prognosis based on the tests, however, is one of degree of renal lesion rather than of duration of life. Duration of life depends on rate of progress of the lesion and the ability of the body to adapt itself to deficiencies in renal excretion, both difficult of foretelling. So until the tests indicate a very marked degree of renal insufficiency we can only surmise in a very loose way as to probable length of life. Repetitions of the tests at intervals gives us some measure of rate of progress, but the course of development of the renal lesion in many cases undoubtedly is one of periods of exacerbation followed by periods of quiescence and little change. This decreases the accuracy of prognostic deductions from tests made at intervals. Still, tests of renal function do aid us materially in forming an opinion as to the probable period of activity of life of our patient and without them this becomes to a larger extent a matter of mere guess-work.

For some time we have been planning the therapeutic management of patients with nephritis on the basis of the evidence from our tests of renal insufficiency. There seems little doubt but that a more appropriate degree of limitation of activity can be made with a knowledge of the condition of renal function. Dietary regulations based on the ability of the kidney to excrete water, nitrogen, and salt as compared with the normal would seem to have



a rational basis. If it is evident that the kidney excretes any of these substances slowly, or if fatigue appears shortly after excretion begins, the deduction made is that an excess of any of these substances in the food intake will overwork the kidney and probably increase the renal damage; on the other hand a decrease in the intake will allow of a rest of renal function with either a gradual increase in power to excrete or a less rapid progression in the renal lesion. This is the hypothesis on which we work in planning a diet based on the ability of the kidney to handle water, salt, and nitrogen. Long experience has indicated that an empirical reduction in intake of salt and nitrogen does benefit the patient. There has been much discussion as to whether water should be increased or decreased. Limitation determined by renal function seems a more rational plan. Further trial and continued observation of patients alone can show how far this is true.

If salt is excreted poorly and there is edema, reduction in salt intake usually decreases the edema if it does not arise from circulatory deficiency, and this benefits the patient. When there is poor salt excretion but no tendency to edema, does a salt excess in the food really act as a renal irritant in any sense? Probably it does, but I do not think our work so far has answered that question definitely.

In the same way if nitrogen elimination is poor a diet low in proteid leads to a decrease in blood urea, and in total blood non-proteid nitrogen and the index of urea excretion appears to improve, but we do not know how much this change really benefits the patient. We do not believe that these nitrogenous substances which we quantitate—urea, uric acid, amino acids, etc.—are injurious in themselves. We assume that when they are poorly excreted the actual toxic substances are retained in the body because in the uremic or toxic state, when presumably they are being retained, we usually obtain high values for non-proteid nitrogen in the blood and have a low index of excretion, indicating defective excretion of nitrogenous substances. We assume that the toxic substance is a nitrogenous body, and so at the same time is poorly excreted. Very likely this is true, but as yet it is only an assumption and should be recognized as such. Decreasing food nitrogen like decreasing food salt very probably leads to renal rest and improvement in renal function, and so to better excretion of toxic substances. Much careful observation, however, is needed as to the effect of dietary limitations on renal function before we can diet rationally our patients with nephritis.

Just the same thing holds with regard to the desirable amount of liquids for a patient with nephritis. In the patient with edema, water reduction is indicated. Without edema we are far from sure how to proceed in the question of the amount of fluid to be given. Observation of the relation between the amount of fluid

intake and urine output helps us, but in some cases definite renal hypersensitivity is present and we do not know the relation that exists between fluid intake and hypersensitivity with regard to renal irritation, and progress in renal damage. Here again much more careful observation is needed.

Our attitude toward dietary restrictions must be interwoven closely with that toward diuretic drugs. Water, salt, and some of the nitrogenous constituents of food are diuretic in their action, inasmuch as they increase urinary excretion. In considering dietary regulations we have emphasized the importance of considering the element of renal fatigue and of renal irritation in determining the advisability of certain dietary limitations. These same factors must be considered in regard to diuretic drugs. The effect of digitalis in improving cardiac function is one of our most brilliant therapeutic effects, and yet we know that with too long-continued doses of digitalis damage to cardiac function quickly results. For digitalis we have quite good indications as to when it is doing damage. Do diuretic drugs have any analogous relations to renal function? May they do damage to renal function? Have we indications of an injurious effect from them?

I have already pointed out that in acute experimental renal lesions we do have considerable evidence that diuretic drugs are harmful and there is very little evidence of a beneficial action. For chronic lesions animal experimentation gives us no satisfactory material for testing, and so we are compelled to base our opinions on observation of patients with chronic nephritis in whom complicating factors render judgment more likely to be fallacious. Diuretic drugs under certain conditions can increase the output of urine. If there is present a considerable degree of edema, theocin and theobromine sodium salicylate will increase the amount of urine in certain patients. In our experience<sup>26</sup> this has been mainly in patients with cardiac insufficiency rather than renal insufficiency. Without cardiac insufficiency, and with renal insufficiency, diuresis in our experience usually does not occur from diuretic drugs even when the edema is marked. This suggests that if the renal damage is in itself sufficient to cause edema, diuretics are unable to stimulate the kidney directly or indirectly to sufficient additional activity to increase the flow of urine. When a diuresis occurs what constituents are increased? Of course the output of water is increased. Some recent observations of ours show that with the increase in water there is a considerable increase in sodium chloride output, but relatively much less of an increased output of nitrogen. The removal of the excess of fluids from the patient's tissues is certainly beneficial, but their removal may not improve renal function. In fact, our observations show that following an active diuresis there

<sup>26</sup> *AM. JOUR. MED. SCI.*, 1915, ci, 635.

may be for a day or two a decrease in renal function as measured by the index of urea excretion. Such a decrease we have seen more often than an increase. Probably this is due to renal fatigue and not to renal damage. Even so it indicates the possibility of harm from over vigorous diuresis. If in the presence of edema, nitrogen output is only moderately increased by diuretics, this should arouse skepticism as to the value of diuretics in patients without edema in whom their toxic condition indicates retention of toxic substances. What evidence have we that diuretics in any way increase the output of these hypothetical toxic substances possibly nitrogenous in nature? It seems to me that we have very little acceptable evidence for this. Although in cases without obvious edema after the use of diuretics we do at times get a considerable increased elimination of fluid and salt; to a less degree of nitrogen, we do not know that this benefits the renal condition. The possibility of doing damage with diuretics always has to be kept in mind. Unlike digitalis we have very unsatisfactory signs of renal damage from diuretics. If a diuresis does not occur it is probable that a continuation in the use of diuretic drugs will work an injury. If a diuresis does occur we are not sure that this is beneficial except insofar as the removal of fluid makes the patient more comfortable. Possibly our tests of renal function may prove very useful in determining benefit or harm from diuretics. At present the factors concerned in diuresis are far too little known and much study of the action of diuretics in chronic nephritis in man are needed before we are prepared to utilize them rationally in the treatment of nephritis. In such a study it would seem that very little help is to be expected from experimental pharmacology. The work must be done on man. With our greatly improved methods of clinical observation, and particularly with our methods of testing renal function, our clinics probably can advance our knowledge of the action and use of diuretics. We must acknowledge frankly the present meagerness of our knowledge of diuretics and approach the problem with both enthusiasm and scientific skepticism. With this attitude I feel that the study of diuretics is an important problem for the clinician to work on. Moreover it gives promise of yielding important results. Certainly, almost any definite knowledge of the laws or principles underlying the action of diuretics will be an addition welcome to all clinicians.

So far I have confined my attention to renal structure and to renal function in relation to diet and diuretics. Other important problems in nephritis are concerned with certain results of the disturbed renal function. In this group come hypertension, uremia, albuminuric retinitis, edema, dyspnea, etc. Of them much study has been made and some of them have been discussed by previous Harvey lecturers, and I can add relatively little to what they already have said to you.

Graphic methods of studying the cardiovascular apparatus have emphasized the early occurrence of hypertension, cardiac hypertrophy, and myocardial disturbance in many cases of nephritis, but they have not thrown much light on the relation between them and the renal lesion. In my own clinic, where we have made much use of the electrocardiograph in the study of the cardiac condition of our cases, I have been impressed with the great frequency of cardiac changes in cases of chronic nephritis and the very great importance of them as causes of the patients' incapacity. Particularly interesting in this connection have been cases in which hypertension seemed undoubtedly the primary condition, myocardial disturbance secondary, and renal insufficiency a negligible feature in the case. Studying the cases we find very slight evidence of impaired renal function, and in a few fatal cases the kidneys have been essentially normal so far as glomeruli and tubules were concerned. There was marked chronic passive congestion of the kidney, for these patients have died from cardiac insufficiency. Arterioles everywhere showed thickening, and therein seemed to be the cause of the hypertension. It has seemed that in this type of case myocardial insufficiency was slower in appearance than in patients with renal insufficiency and hypertension. All clinicians are familiar with this type of patient, but it seems to me that they are probably more numerous than we have supposed, because without studying their renal function we have assumed them to have a more extensive renal lesion than they do, and so classified them among our cases of chronic nephritis when really they did not belong there. Possibly a more careful study of this group may throw some light on the mechanism of the hypertension in chronic nephritis.

None of our studies have been concerned with the cause of uremia. Its importance is obvious, but none of our group of workers has possessed the chemical knowledge needed for such a study. The primary problem in uremia is to know the nature of the toxic substance that causes the uremic manifestations. Important studies have been made on the problem in other laboratories, but not yet have they advanced to the point of giving us a means of recognizing toxic substances and studying their distribution and effects as a part of the problem of the clinical study of nephritis.

In our cases Woods<sup>27</sup> has made a careful study of the eye-grounds to see if any relation between albuminuric retinitis and renal function could be found. It has been claimed by Widal and his co-workers<sup>28</sup> that albuminuric retinitis was closely related to nitrogen retention. To see if this were true the total non-protein nitrogen of the blood was determined in a group of cases and the figures obtained tabulated along with the changes observed in the retina. Naturally, since in cases of severe nephritis retinal changes are

<sup>27</sup> Arch. Int. Med., 1915, xvi, 577.

<sup>28</sup> Ann. d'ocul., 1910, exiii, 354.

more common than in mild cases, our cases with high non-protein nitrogen figures showed retinal changes more often than those with low figures. However, there was no relation to be made out between the retinal disturbance and degree of nitrogen accumulation in the blood. To see whether there was any parallelism between the occurrence of retinitis and the amount of various forms of nitrogenous bodies in the blood, determinations of urea, uric acid, creatin, creatinin, ammonia, and amino-acid nitrogen were made but no relationship could be found to exist. It was thought possible that some relation might exist between the amount of non-proteid nitrogen in the spinal fluid and retinal changes, so this was determined as well as the urea content of the spinal fluid; but here again no relationship was found. It was interesting to see how closely parallel to each other ran the urea values for blood and spinal fluid, there being very slight differences between the two, while for total non-protein nitrogen the amount in spinal fluid lagged very considerably behind that in the blood. Not enough spinal fluid was available for determination of the other nitrogenous bodies which we quantitated in the blood.

The dyspnea of nephritis is of much interest; often it is a very distressing symptom in our patients. It presents itself in many forms. Very often it is paroxysmal with a proneness to nocturnal attacks. Periodicity commonly is a feature, often of the typical Cheyne-Stokes type. In other cases the dyspnea is present almost continuously. In a few cases it is of the slow, deep variety, the air hunger type, such as we see in association with diabetic coma. In many patients the dyspnea in large part is associated with the cardiac insufficiency, which is marked as a condition due to the hypertension and myocarditis secondary to the nephritis. In other cases the cardiac element is slight or absent. In our clinic, Peabody<sup>29</sup> has studied the relation of the dyspnea to acidosis, as this has been claimed by some to be the chief factor in the production of the non-cardiac dyspnea of chronic nephritis. Peabody found that in mild cases of nephritis there was no evidence of acidosis. More advanced cases show an acidosis in the sense that much larger amounts of alkali are required to render the urine alkaline in reaction than is normally the case. Such patients, however, show no decreased  $\text{CO}_2$  tension in the alveolar air. It is only in the very advanced cases that acidosis becomes marked enough to cause a decreased  $\text{CO}_2$  tension in the alveolar air. The evidence at hand favors acid retention in these cases of nephritis rather than an abnormal formation of acid. The usual type of dyspnea in nephritis is a periodic breathing of an irregular shallow type, and this will persist after the giving of an alkali has rendered the urine alkaline and restored the  $\text{CO}_2$  tension to a higher value. In some cases the

<sup>29</sup> Arch. Int. Med., 1914, xiv, 236; and 1915, xvi, 955.

dyspnea is of the "air hunger" type, and this may disappear after giving alkali. Acidosis does not seem to be a sole factor in any sense in the usual dyspnea of nephritics who have no cardiac insufficiency. It probably has some influence, but other factors undoubtedly are active. Very likely variations in the sensitivity of the respiratory centre play an important part. If the respiratory centre is abnormally sensitive then very slight changes in the blood may be effective under these abnormal conditions, and both changes in the respiratory centre and in the blood are concerned in the dyspnea of nephritis.

What I have presented is far from a complete account of the very many interesting phases of the nephritis problem. As I stated in the beginning, I have made it fragmentary by limiting my discussion to those phases on which my associates and myself have worked. I have purposely refrained from presenting tables, figures, and statistics, as such details are so difficult to keep in mind while listening to a paper. They may be found by those especially interested in the individual reports of our work, which have been published in current medical journals since 1908 and for which references are herewith given. If I have succeeded in rekindling any interest in the fascinating problems of nephritis by presenting this account of our work, my purpose has been fully accomplished.

## THE SURGICAL SIGNIFICANCE AND OPERATIVE TREATMENT OF ENLARGED AND VARICOSE VEINS OF THE SPINAL CORD.<sup>1</sup>

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A STUDY of the literature of the subject will show that abnormalities of the arteries of the spinal cord have been found post-mortem in a number of instances. Haberer<sup>2</sup> has described a case of congenital obliteration of the aorta with a collateral circulation formed by means of the spinal arteries. Aneurysm of the posterior spinal vessels as the cause of spinal symptoms was found on autopsy in the patients of Brasch,<sup>3</sup> Raymond and Cestan,<sup>4</sup> and

<sup>1</sup> Read at the meeting of the American Neurological Association, New York, June, 1915.

<sup>2</sup> *Ztschr. f. Heilk.*, 1903, N. F., 4, xxvi.

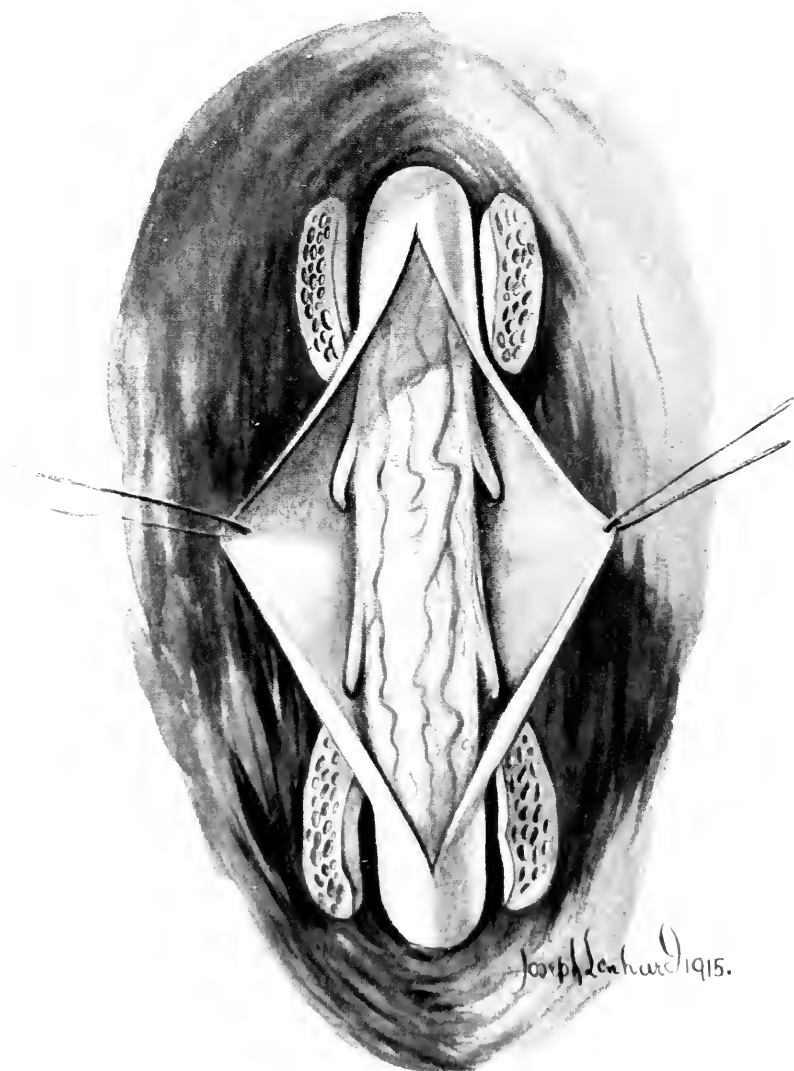
<sup>3</sup> *Berlin, klin. Wchnschr.*, 1900, 52 and 53.

<sup>4</sup> *Revue neurologique*, 1902.



FIG. 1

A

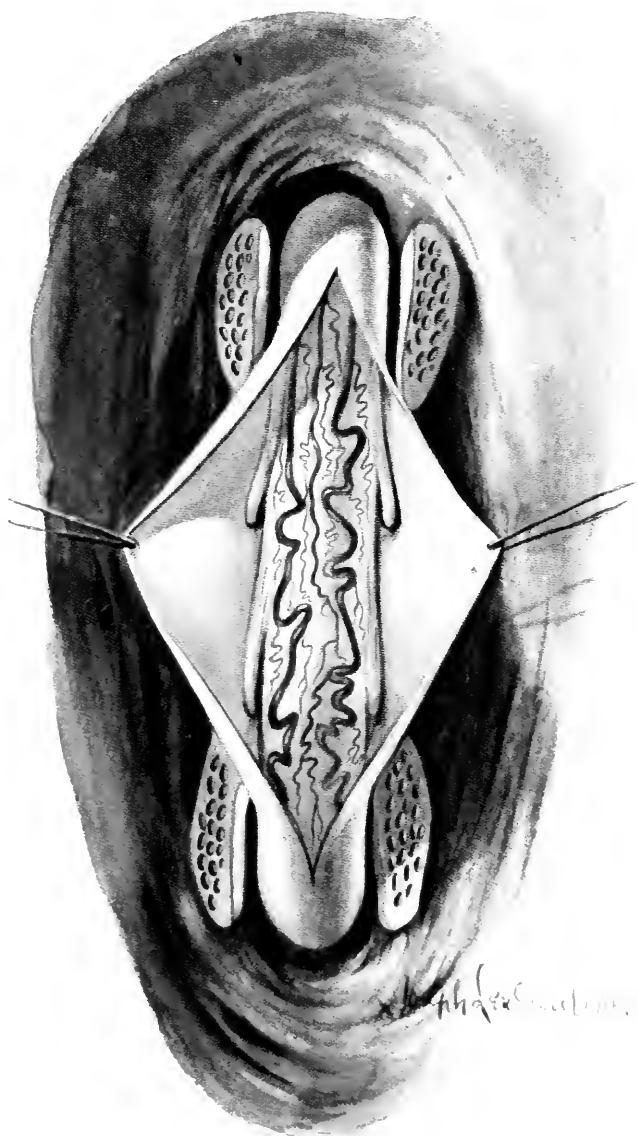


Hyperemia of the Spinal Cord in Meningitis



FIG. 1

B



Venous Engorgement below the Level of an Extra-medullary New Growth



Heboldt,<sup>5</sup> and at operation by the writer.<sup>6</sup> Angioma of the cord was the lesion found by Gaupp, Lorenz, and Barenbruch. The last two authors mentioned do not make it clear whether the vascular disease affected the arteries or both arteries and veins of the cord.<sup>7</sup>

Surprisingly, little has been written on abnormal conditions of the spinal veins; for this reason it has seemed to me worth while to describe certain peculiarities of the veins which I have observed in the course of a large number of operations upon the spinal cord.

As is well known, there are two main posterior spinal veins which run on the posterior surface of the cord from the conus medullaris to the medulla. These two veins are, normally, somewhat tortuous; they lie superficial to the origins of the posterior spinal nerve roots and communicate with each other by means of small branches. The main trunks are joined by small veins from the posterior spinal roots.

1. THE DIAGNOSIS OF SPINAL COMPRESSION FROM THE APPEARANCE OF THE VEINS BELOW THE LEVEL OF THE PRESSURE. The posterior spinal veins are sometimes considerably enlarged below the level of a spinal compression. On account of interference by the pressure of an extramedullary neoplasm with the return venous flow, the veins become much enlarged and engorged with blood for a considerable distance below the level of the tumor. When the cord of such a patient has been exposed, one or both veins appear very large and very prominent; they are often more tortuous than normal. In intradural inflammatory processes—meningitis and meningomyelitis—the cord has a pink color due to the fine network of distended arteries and veins in the hyperemic area. The appearance is not the same as that below a spinal compression in which distended veins stand out prominently on the creamy-white background of the cord. (See Fig. 1, *a* and *b*.)

In several patients upon whom I performed a laminectomy for a spinal tumor, and did not find the growth at the suspected level, this venous engorgement led me to search for the growth higher up. In one instance I had to remove five additional vertebral arches before the tumor was exposed and removed.

It is important, therefore, for the operator to recognize and to understand the significance of these distended posterior spinal veins and to differentiate a venous engorgement due to pressure from an ordinary inflammatory hyperemia of the cord.

2. LOCALIZED ENLARGED AND VARICOSE VEINS OF THE CORD. More or less localized enlargement or varicosity of one or both posterior spinal veins is a condition which is not very rare; it may

<sup>5</sup> Archiv f. Psychiat., xvi, 813.

<sup>6</sup> Surg., Gynec. and Obst., 1913.

<sup>7</sup> Recently Cobb (Annals of Surgery, December, 1915) has described a case of "hemangioma of the spinal cord." From the description given by the author, the case is very like those of Gaupp, Lindeman, and Krause.

be the cause of local spinal symptoms, and complete relief from the symptoms may follow an operative interference.

Up to the year 1912 four cases had been reported in medical literature in which compression of the spinal cord by enlarged spinal veins had occurred. Gaupp<sup>8</sup> described a case of what he termed "hemorrhoids of the spinal pia mater," in which the lumbar cord was compressed by the dilated and tortuous vessels. Jumentie and Valensi<sup>9</sup> describe the postmortem appearances of the spinal cord in a patient with complete paraplegia. On the posterior surface of the cord, between the lower cervical and middle dorsal segments, there were numerous dilated veins. Some of these veins accompanied the nerve roots to the dural openings. Finally, Lindemann<sup>10</sup> describes a case of varices of the vessels of the spinal pia mater and the cord as the cause of a total transverse lesion. The patient had the signs and symptoms of a slowly progressive transverse lesion of the cord of two years' duration, and succumbed to decubitus and sepsis. At the postmortem examination the veins on the posterior surface of the cord, beginning about 7 cm. below the cervical enlargement, were much dilated and very tortuous, so that they caused a marked flattening of the cord.

The case described by Krause<sup>11</sup> is the only one in which the abnormality of the spinal vessels was found on the operating table. Krause's patient presented the symptoms of an intravertebral growth of seven years' duration which had caused a complete paraplegia. At the operation he found a mass of dilated veins, some of which entered the cord at the level of the ninth to the twelfth dorsal vertebrae. The operator was able to ligate a number of the vessels, but the patient did not improve, and death occurred three months later.

Among 130 laminectomies for spinal disease I have 6 times found one or several enlarged spinal veins on the posterior surface of the cord. In all but one of the patients the enlarged vein ran a straight course; in several instances the enlarged vein accompanied one of the spinal roots to the dural opening. (See Figs. 2 and 7.) All of the patients had the signs and symptoms of a level lesion, and the greatest or only enlargement of the vein was found at the part of the cord which corresponded with the symptoms. Two of the patients suffered from severe root pains and large veins were found to accompany the affected spinal roots.

As soon as the laminectomy had been performed and the dural sac had been incised the enlarged vein stood out prominently. In all of the patients the left posterior spinal vein was enlarged; it was three to six times the size of the vein on the right side, and

<sup>8</sup> Beitr. z. path. Anat. u. z. Allg. Path., 1888.

<sup>9</sup> Revue neurologique, 1911, xix, 81.

<sup>10</sup> Ztschr. f. d. ges. Neurol. u. Psychiat., 1912, xii, 522.

<sup>11</sup> Chirurgie des Gehirns und Rueckenmarks, 1911, p. 775.

sometimes ran an abnormal course. The enlarged vessel sometimes ran underneath or around one or more nerve roots. (See Fig. 3.)

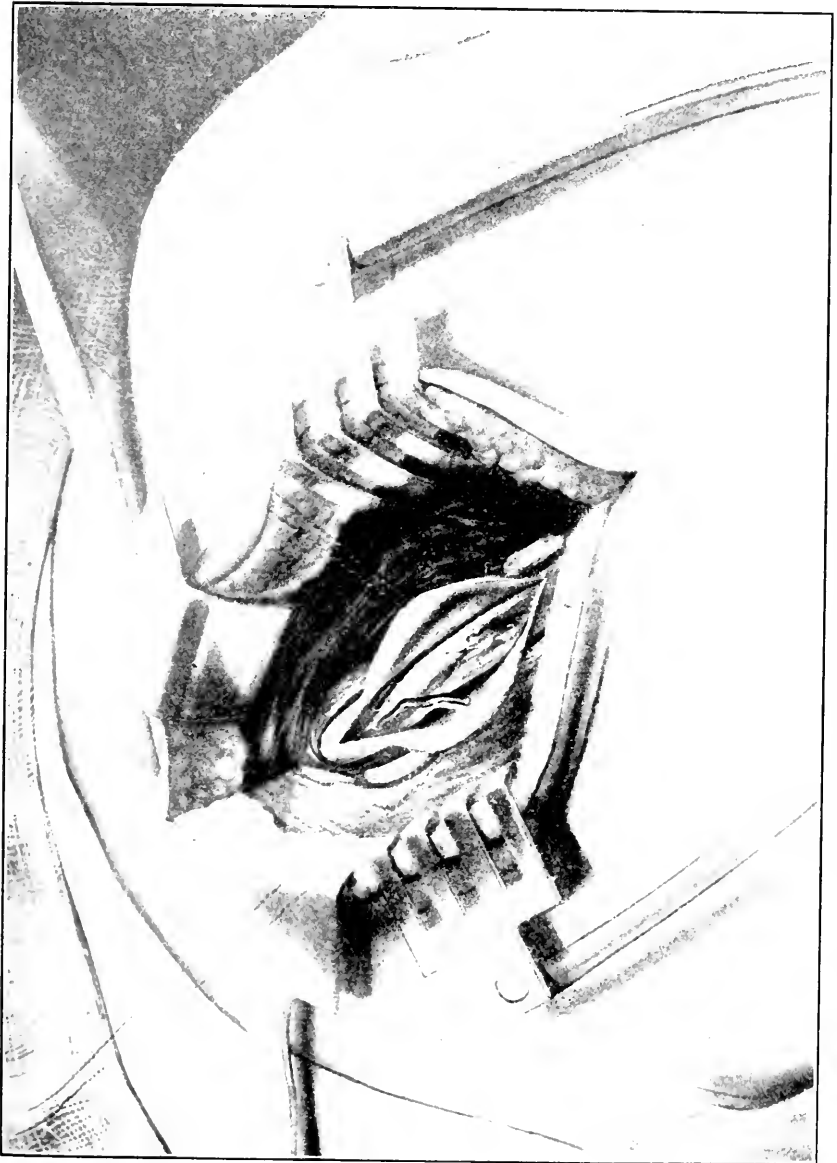


FIG. 2. Enlarged vein which accompanied the left eighth posterior spinal root and caused severe root pains.

In one case the vein was very tortuous (Fig. 4), so that it could fairly be called "varicose;" in another instance (Fig. 2) only the branch of the vein which accompanied the nerve root at the level

was enlarged. In still another instance a branch of the large vessel—itself three or four times as large as normal—entered the substance of the spinal cord near or in the posterior median septum.



FIG. 3. Enlarged posterior spinal vein which ran an abnormal course in relation to two posterior nerve roots.

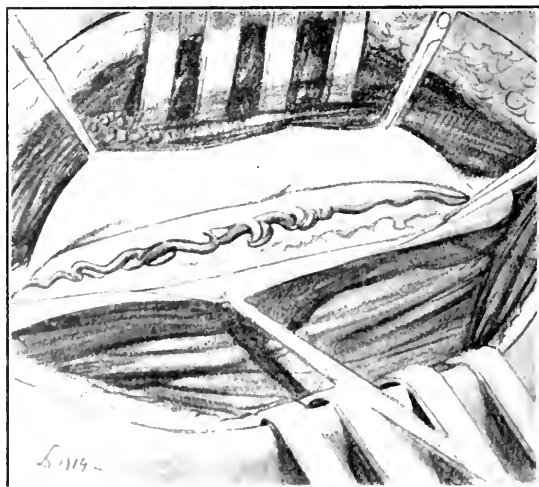


FIG. 4.—Varicose vein of the spinal cord.

The abnormal vein lay in the dorsal region in five and in the lumbo-sacral region in one case.

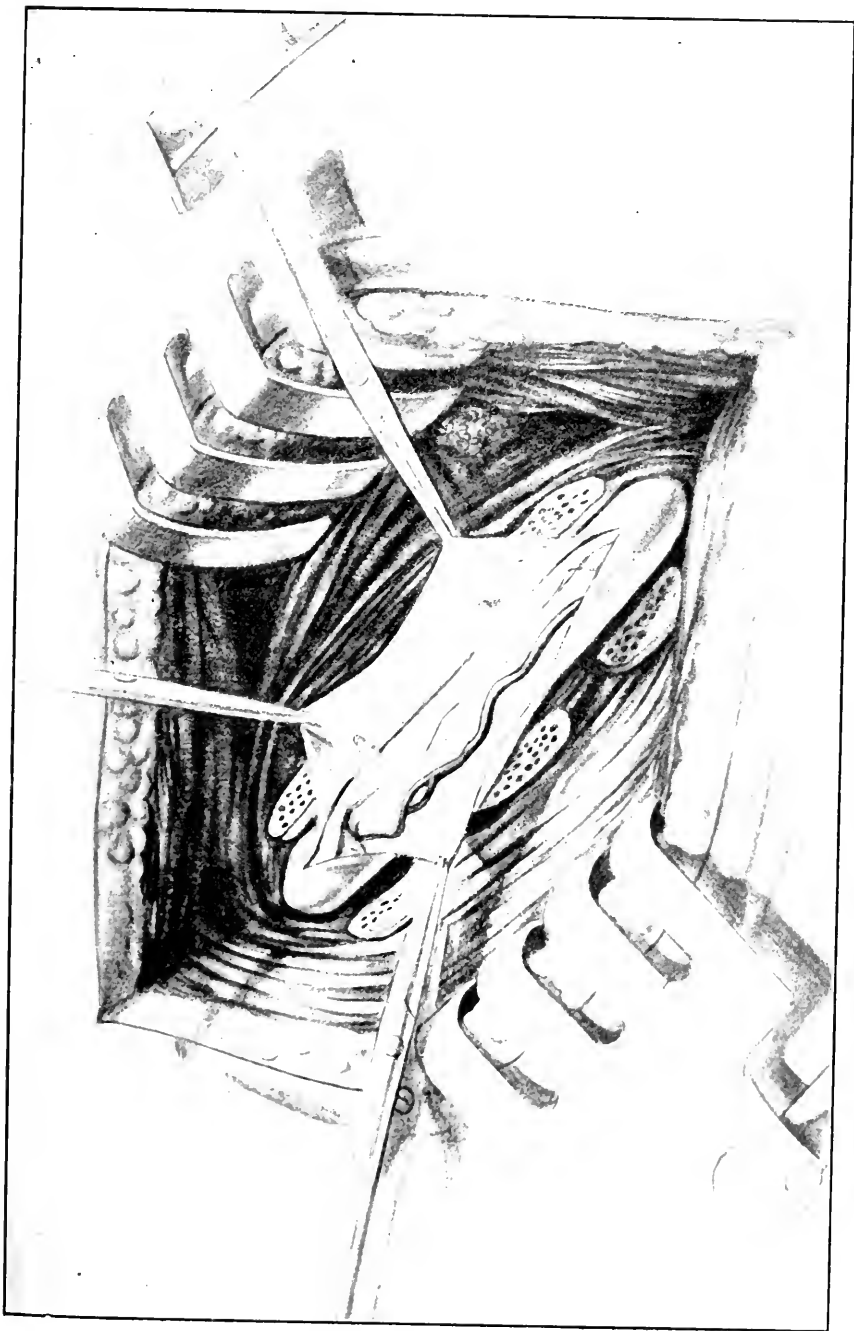


FIG. 5. Enlargement of the left posterior spinal vein in a patient with symptoms of spinal tumor.

In all of the patients the greatest or only enlargement of the vein was found at the level of the symptoms, and on the side on

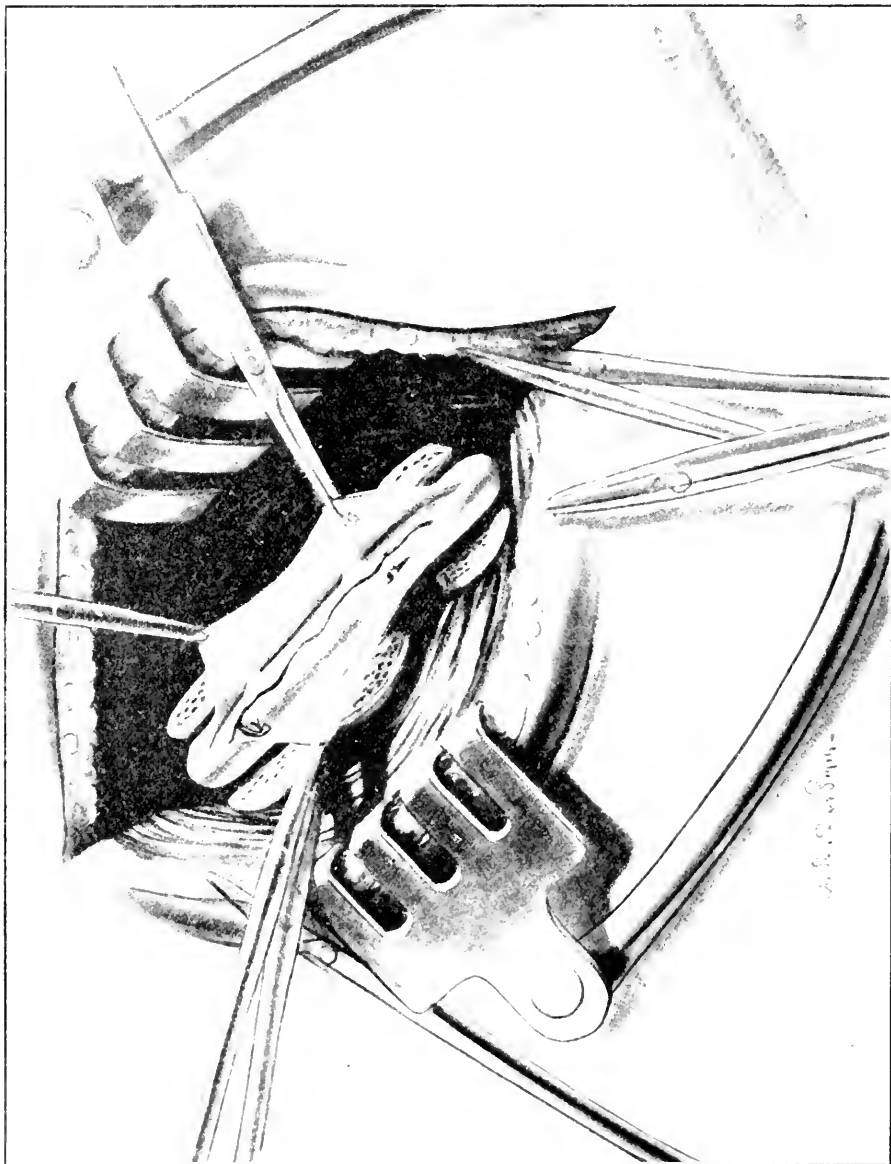


Fig. 6.—Appearance after ligation and excision of part of the vein shown in Fig. 5.

which there had been root pains. It is fair to conclude, therefore, that there was some connection between the enlargement of the vein and the cord symptoms. Whether the venous enlargement



was the primary condition and the cord disease was secondary, whether the reverse was the case or whether both played a part

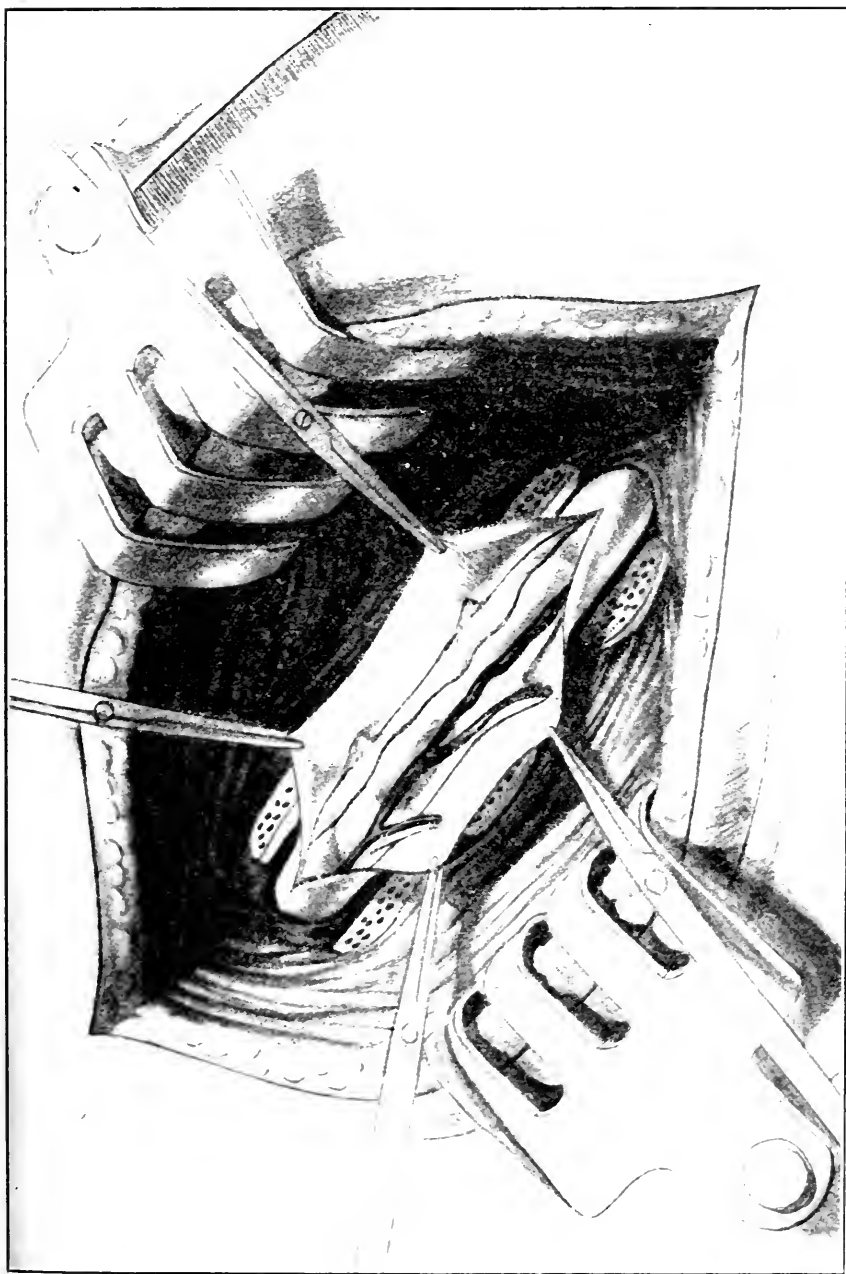


FIG. 7. Enlarged left posterior spinal vein overlying an intramedullary tuberculoma of the cord. Large branches of the vein ran with the 11th and 12th nerve roots. The patient had very severe root pains over the distribution of the lowest dorsal roots.

in any of the patients it is impossible to say with certainty. In two the symptoms and signs were so similar to those of a spinal tumor that a probable diagnosis of spinal tumor had been made. In one patient the enlarged vessel lay in the general region occupied by a tuberculoma which was successfully removed from the substance of the lower dorsal cord.

The discovery of the enlarged or varicose vein was in each instance an operative finding. That the abnormality was not temporary, perhaps due to the exposure of the cord and the change in pressure conditions, was proved by the fact that the spinal vein of the other side always appeared normal in size and position. Up to the present time only one excised vein has been subjected to a

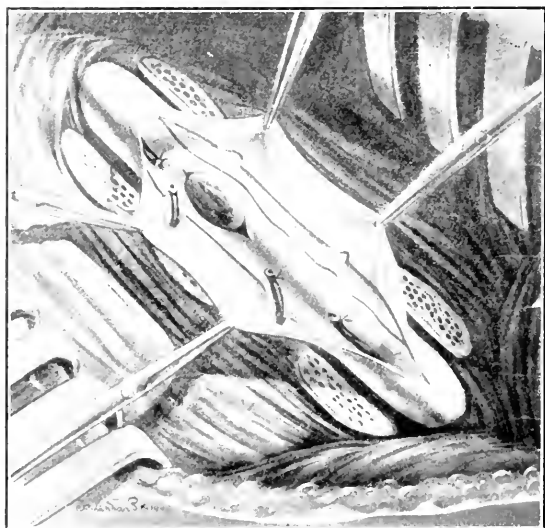


FIG. 8. The vein has been ligated and part of it excised. The tumor has been partly delivered from the cord.

microscopic examination. Dr. Leo Buerger, to whom I am indebted for the examination of the specimen, reported that there was a "hyaline degeneration of the vessel walls."

I have made it a practice to excise as much as possible of the enlarged vein, although I am not prepared to say that this is necessary in all instances. (See Figs. 5 and 6.) The enlarged vein can usually be raised up from the cord by means of a strabismus hook, and ligatures of fine silk can be passed around the vessel by means of a small aneurysm needle. These veins are very fragile, and one must be very careful that the vessel is not torn during the manipulations. If the veins of one or more posterior roots are enlarged the vessels should always be excised down to the dural openings.

I have described these abnormalities of the veins as interesting operative findings; we know nothing of their significance. It remains to state what results were obtained in the patients in whom enlarged veins were found and excised. Of the six patients, two had a spastic paraplegia with sensory level symptoms of long standing, and their condition was unchanged after the operation.<sup>12</sup> The patient with a tuberculoma of the cord (Figs. 7 and 8), improved very much, but the improvement was, without doubt, due to the removal of the growth. A patient who had suffered from severe root pains confined to the distribution of the left eighth dorsal root, and in whom a much enlarged vein ran with the root, was entirely relieved by the laminectomy and excision of the large vein.

Two patients were suspected of a spinal tumor, but nothing excepting the localized venous enlargement was found at the operation. Both of the patients had well-marked sensory and motor signs, and marked improvement followed the surgical interference. One of the patients recovered entirely; his history is given in some detail in what follows:

**CASE HISTORY.**—A Turk, aged twenty-three years, was admitted to the neurological service of Mount Sinai Hospital on the service of Dr. B. Sachs in October, 1914. The patient complained of cramp-like pains in the left side of the abdomen, running down the left lower extremity, of three months' duration. With this there had occurred symptoms of increasing loss of power and spasticity in the lower extremities.

Physical examination showed that the abdominal reflexes were absent on the right side. The knee-jerks were more exaggerated on the left side than on the right. There was no clonus or Babinski. The left leg was weaker than the right. There was slight tenderness of the spinous processes of the ninth dorsal vertebra. Wassermann test and Roentgen rays were negative.

The symptoms gradually grew worse, so that one week later there was a slight Babinski on the left side, with exhaustible ankle-clonus and spasticity of the left lower extremity. The sensory signs consisted of almost complete loss of pain, temperature and tactile sensation of the right lower extremity up to the level of the ninth dorsal segment. The symptoms, therefore, pointed to a focal lesion, probably in the left anterolateral region of the cord between the eighth and ninth dorsal segments, and the patient was transferred to my service for operation.

Laminectomy was performed (Dr. Elsberg) on October 16, 1914. The spines and laminae of the seventh, eighth, and ninth dorsal vertebrae were removed in the usual manner. When the dura was opened a considerable amount of cerebrospinal fluid escaped, and the surface of the cord was seen to be normal in appearance. The

<sup>12</sup> March, 1916. One of these patients has improved so much that he is able to walk around without assistance.

fifth and sixth dorsal arches were then removed and the dura incised in an upward direction. It was then seen that the right posterior spinal vein ran a normal course, while the left was much enlarged and ran together with the eighth left posterior root through the opening in the dura. The vein was almost again as large as the nerve root. (See Fig. 2.) The vessel was ligated at the dural opening and about 2 cm. of it was excised. The wound was closed in the usual manner.

Convalescence was uncomplicated. The patient was out of bed in two and a half weeks; the symptoms of spinal disease grew less and less distinct; by the beginning of November all of the sensory and most of the motor symptoms had disappeared. Three months after the operation he was entirely well, and he was well when last heard from about six months after the operation.

It may be that this remarkable result was due to the decompressive effect of the laminectomy. Pearce Bailey and I have shown that the free opening of the spinal canal and the entrance of air into the subdural space has a striking influence upon the spinal cord, and may, and often does, affect some change which temporarily or permanently benefits or checks the symptoms of local spinal disease. This may be the explanation for the postoperative course in several of our patients.

## THE ROLE OF THE SYMPATHETIC SYSTEM IN THE DIAGNOSIS OF ABDOMINAL DISEASES.

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WHEN we see a patient with the following classical history: sudden epigastric or umbilical pain—followed by vomiting—later the pain becoming localized in the right lower quadrant of the abdomen, the right rectus muscle becoming rigid over the painful area, then we palpate, find tenderness at or about McBurney's point, make the diagnosis of appendicitis and commonly conclude that the tenderness experienced is due to pressure by the finger on the diseased organ. If, however, we operate, the appendix is very often found not under the point where pressure was exerted, but some varying distance therefrom. Similarly in disease of the gall-bladder, pressure exerted over the organ causes pain, which pain is increased when the gall-bladder is made to descend by deep inspiration. If the diseased gall-bladder is exposed it may be handled in various ways without giving rise to the sensation pain.

It is tempting and may be profitable to hunt for some reasonable explanation of the sequence of symptoms in such a disease as

appendicitis, where so many of the symptoms seem unconnected with the organ at fault, and also to endeavor to find some explanation why a chronic appendicitis may give rise to symptoms which must be attributed by the clinician to gastric ulcer which is found to be non-existent on exposure of the stomach.

The convenient expression "reflex pain," is too often used as a cloak to cover our ignorance, and often when using it we forget, if we ever knew, what constitutes a reflex pain.

Originally the gastro-intestinal canal was a straight tube developed in the dorsal region and pushed into the primitive body cavity in such a fashion that it became enveloped with peritoneum but retained its connection with the dorsal structures by means of bloodvessels and of nerves which lay between the layers of the primitive mesentery. From the original straight tube there developed the liver, pancreas and spleen near the dilated portion of the tube which came to be the stomach. As development proceeded the various organs assumed the positions in which they are found in the normal individual. Thus we see that the vascular and the nerve supply of each and every part of the digestive tract was arranged as if these viscera were to retain a position in the middle line. The viscera ultimately normally take up positions which may be remote from the middle line, yet their telephone supply remains the same except for the necessary elongation of the wires. This may explain why the early pain of most visceral lesions is generally median.

What is the nerve supply of the gastro-intestinal tract? The nerves of the abdominal viscera pass to a very large extent into the solar or celiac plexus, which is a congeries of nerve filaments and ganglia (special ganglia in it are the right and left semilunars). The solar plexus is connected above with the aortic plexus of the thorax and below with the abdominal aortic plexus, etc. By the splanchnic nerves it communicates with the gangliated sympathetic cord and so with the anterior primary divisions of the spinal nerves. The plexus is connected with the cranial nerves through the pneumogastric route. The left vagus, distributed to the anterior surface of the stomach, only anastomoses with a branch from the left semilunar ganglion in about 25 per cent. of cases. This anastomosis recalls to a certain degree the loop of Wrisberg, formed by the union of the right vagus and great splanchnic nerves. The anterior gastric plexus may sometimes anastomose with the sympathetic surrounding the left diaphragmatic artery (Poirier and Charpey). The right vagus, after giving some branches to the esophagus, enters into the right semilunar ganglion, where it loses its anatomical identity. While the vagus has no connections with the cephalic sympathetic it gives the most important parts of its fibers to the ganglia on the visceral branches of the sympathetic (Wrisberg's, intracardiac and semilunar ganglia). These ganglia are the true nodal

points of junction between the pneumogastric and sympathetic systems, beyond which the nerves are anatomically inseparable.

Another connection of the plexus must be considered, viz., that with the phrenic nerves. The anatomy of the phrenics themselves is important from a clinical standpoint.

The principal fibers of the phrenic nerves come from the fourth cervical, but the third and fifth cervical nerves provide secondary roots. In the thorax the phrenic sends branches to the pleura, pericardium and diaphragm. Most of the pericardial branches come from the right nerve. This is important as explaining how pain in the *right* shoulder arises through impulses transmitted through the supra-acromial branch of the fourth cervical nerve.

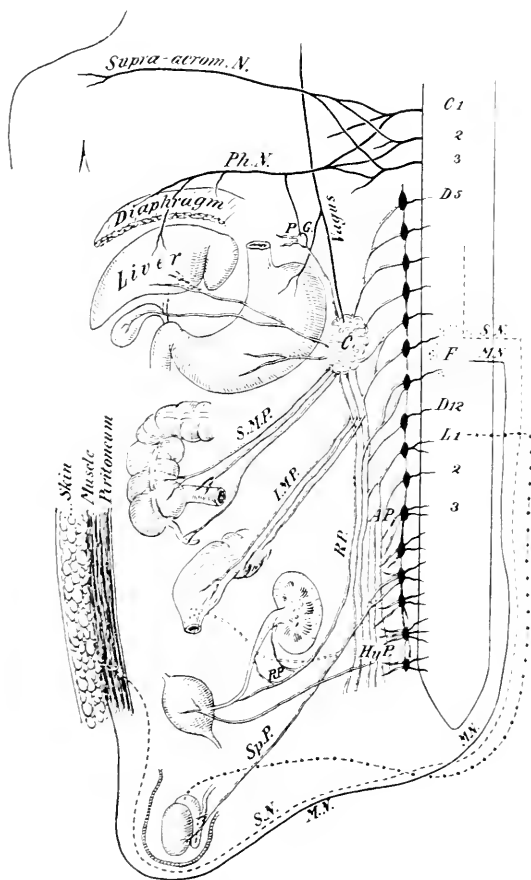
The right phrenic besides innervating the diaphragm sends fibers to the liver and to the anterior parietal peritoneum as low as the umbilicus. Luschka thinks the peri-umbilical pain in peritonitis is due to excitation of these last-mentioned fibers.

Another branch of the right phrenic, uniting with the phrenic ganglion and fibers of the sympathetic, helps to form the diaphragmatic plexus, which also receives branches from the five lowest intercostal nerves. The left phrenic has no connection with the phrenic ganglion but sends a few twigs to the left semilunar and solar ganglia. Probably irritation of the right phrenic nerve is the explanation of the anomalous symptoms found in a woman, aged twenty-one years, who came to me complaining of severe pain in the right abdomen. From childhood she had been troubled with nausea and vomiting, without pain, coming on from a few minutes to an hour after meals. Sour eructations were occasionally present. Hunger distress at night or in the early morning was frequently noticed. In recent years and when seen she frequently suffered from a feeling as if the liver were a heavy weight pressing on her right side when she lay on that side and dragging on the right side when she lay on her left side. Three weeks before I saw her there was an attack of severe abdominal pain in the hepatic region accompanied by fever of  $102^{\circ}$ , slight jaundice, and clay stools. Three days before admission to hospital pain in the hepatic region returned, there was a slight chill and a temperature of  $103^{\circ}$ . There was a slight hacking cough without sputum. The pain was all over the hepatic area and extended to the angle of the right scapula. There was exquisite tenderness over the region of the gall-bladder and appendix. The right chest gave the ordinary signs of empyema. Thoracotomy was followed by complete disappearance (temporary at least) of all the abdominal symptoms.

Every surgeon remembers how routine examination of the chest has saved him from operating for intestinal obstruction when pneumonia was the cause of the menacing symptoms.

The stimuli from the disease, in such cases, seem to affect the phrenic or lower intercostal nerves, giving rise to abdominal pain, rigidity, etc., to such a degree as to be most deceiving. The accom-

panying diagram shows roughly the connections of the solar, superior and inferior mesenteric and the spermatic plexuses. The apparent functions of the visceral nerves are (1) to transmit afferent stimuli to certain centers from which (2) efferent impulses are sent to the viscera. The efferent impulses stimulate or inhibit peristalsis, secretion, etc., in the organs in response to the needs of the body as communicated by means of the afferent impulses. The nerve



*Ph. N.*, phrenic nerve; *P. G.*, phrenic ganglion; *C.*, celiac or solar plexus; *S. M. P.*, superior mesenteric plexus; *I. M. P.*, inferior mesenteric plexus; *R. P.*, renal plexus; *A. P.*, aortic plexus; *Hy. P.*, hypogastric plexus; *Sp. P.*, spermatic plexus; *C.*, 1 2, cervical nerve roots; *D.*, 1-2, dorsal nerve roots; *S. N.*, sensory nerve; *M. N.*, motor nerve; *F.*, area of stimulation in cord.

centers in question carry on these functions without the cognizance of the higher brain centers.

If, however, owing to local conditions, *e. g.*, inflammation or any irritation, there is sudden and great increase in the number of stimuli passing up from any viscus then the nerve center is incapable of

handling the increased volume of material, and there is radiation of the impulses in all directions.

According to Mackenzie, who has written much on this subject, the radiating impulses stimulate or affect neighboring nerve centers or tracts. These nerve tracts may be the trunks of sensory nerves passing up the spinal cord from distant parts and the stimuli applied in their course pass up to their cerebral centers and are translated into terms of pain, but the pain is thought to come from the end of the nerve and not from the point in which the stimuli actually originated. This is a referred pain.

In the same way the radiating stimuli may affect a motor path—pass down to the muscles supplied by the path and cause contraction or rigidity of these muscles.

Let us take a concrete clinical example. In appendicitis an abnormal volume of stimuli passes from the appendix through the superior mesenteric to the preaortic plexuses, reaches the spinal cord and there radiates. If a sensory nerve or nerve cell is irritated by the radiating impulses pain is experienced and is located in the territory of distribution of that nerve; in the case of the appendix this is near McBurney's point.

Head expresses the same notion as follows: "When a painful stimulus is applied to a part of low sensibility in close central connection with a part of much greater sensibility, the pain produced is felt in the part of higher sensibility rather than in the part of lower sensibility to which the stimulus was actually applied." In the same way "when from any cause one or other of the cutaneous senses is depressed in a given area stimulation in this region may give sensations which are referred to the symmetrical area on the other side of the body, or if this also is involved, it may be referred to the area next above or below in the spinal order." (Howell.) To this peculiarity the name of *allochiria* has been applied.

Stimuli from the appendix center constantly acting on the sensory nerve or its receptors, keep it in a constant state of irritation, so that if its distal terminals are stimulated, *e. g.*, by palpation, etc., there is distinct tenderness experienced. Such irritability of nerve cells gives rise to the hyperalgesic zones of Head and McKenzie.

Head and Rivers have shown that in the skin there are two systems of sensory fibers, viz., the protopathic and epicritic. Protopathic sensibility responds to extremes of heat and cold, to pain, to pressure, etc.

Another set of nerves (system of deep sensibility) conveys sensations of deep pressure and pain, localizes pressure, and tells of alterations in the position of joints, muscles and tendons. It may be described as a rough index of sensation. Epicritic sensibility is confined to the skin and responds to small differences in temperature, to light pressures, and gives tactile discrimination.

The sensory nerves provide separate fibers for the reception of stimuli of pain, heat, cold, light pressures, etc. The cutaneous



senses are distributed in a punctiform manner. Thus in appendicitis ordinary palpation gives rise to pain through a rather widespread stimulation of the nerve endings in the deep structures and of both the protopathic and the epicritic systems in the skin. Light stimulation of the skin, as by brushing with cotton or by gentle pinching, causes pain through the epicritic system alone—the stimulus being too delicate to affect the protopathic nerves. Pricking the skin with a pin affects the ending of an individual nerve fiber and causes either a protopathic or an epicritic pain. It is perfectly conceivable that there may be excessive excitability to a light brushing with cotton or to palpation and diminished excitability to the definitely localized stimulus of a pinprick. Sherren has corroborated and extended the work of Head as it applies to appendicitis. He writes: "In appendicitis cutaneous hyperalgesia varies from a complete band extending on the right side from the middle line below the umbilicus in front to the lumbar spines behind, down to a small circular spot a little above the middle point between the umbilicus and the anterior superior spine. This band corresponds to the eleventh dorsal area of Head. Very often the tenderness extends somewhat into the tenth dorsal area also and occasionally, but not often, into the twelfth dorsal area, sending a tongue-shaped process over the gluteal region." The usual area of hyperalgesia is triangular in shape and situated in the right iliac region. Occasionally the hyperalgesia is bilateral, it is never on the left side alone, and it does not vary with the site of the appendix.

Sherren, Moullin and others, particularly of the London Hospital School, consider disappearance of cutaneous hyperalgesia with persistence of the other symptoms of appendicitis to be significant of gangrene or perforation. Metzger found that hypoesthesia to a pinprick is rarely absent in the prececal region during appendicitis, and argued that the abdominal reflex being dependent on the perceptive sensibility of the pain nerves, any decrease in their sensitiveness must lead to diminution or loss of that reflex. Whether Metzger's argument is correct or not there is no doubt as to the frequent presence of hypoesthesia to pinprick and the absence of the abdominal reflex. The presence of superficial hyperalgesia to gentle stroking is often a really valuable symptom in appendicitis.

Just as radiating impulses can stimulate sensory nerves so also may they affect motor nerves, and we have rigidity of muscles in the abdominal walls. The stimulation of any individual bundle of nerve fibers as it leaves the cord to go to one of the flat abdominal muscles causes contraction of the individual muscle fibers supplied by it and not of the whole muscle. The muscular contraction which results from a visceral stimulus may remain for an indefinite period and cause a tumor-like swelling. In cases of appendicitis where the examiner believes that he can palpate the appendix it is usually such contracted muscular fibers which he feels, and as there is also

present hyperalgesia of the muscle, the patient complains of pain and thus tenderness of the vermiform appendix is erroneously believed to be present.

Undoubtedly many of the so-called phantom tumors of the abdomen have an origin similar to the above

Mackenzie and his disciples believe that the abdominal sympathetic nerve centers are incapable of the perception of pain and that all visceral pain is of the nature of a viscerosensory reflex as described in the preceding paragraphs. This doctrine is very satisfactory in explaining many otherwise obscure symptoms, but it seems to ignore many important facts.

Mackenzie speaks of the pains due to increased peristalsis of the small intestine as being median and umbilical or epigastric; of the large intestine as being median but lower in site; of the stomach as being median and high in the epigastrium. The viscerosensory theory is a soul-satisfying explanation of the late pains in visceral disease, *e. g.*, at McBurney's point in appendicitis, but it fails utterly to explain the early median pains common to appendicitis, intestinal colic, etc. What reasonable explanation can be given for the median site of these pains and for the undoubted fact that the pains due to cholecystitis, to gastric and duodenal lesions, and to appendicitis may each closely or exactly simulate one of the others?

Several explanations may be given, each of which is open to criticism. Probably the truth may be found in some combination or modification of these explanations.

While the stimuli from a normal vermiform appendix can pass through the solar plexus to their proper center in the spinal cord, the greatly increased stream of stimuli from an inflamed appendix fails to be accommodated by the normal passageway through the plexus, and thus being prevented from free passage gives rise to a general solar-plexus disturbance. The most common cause of a general solar-plexus disturbance is the presence of some irritating substance in the stomach and small intestine, and the customary motor response is an endeavor to get rid of the irritant by increased peristalsis. The increased peristalsis is accompanied by pyloric spasm, hence vomiting. The pain of increased peristalsis is median and high up. Opinions differ much as to the power of the receptors of the gastro-intestinal nerves to appreciate pain. It is undoubtedly true that we can operate upon and can even maltreat exposed viscera without inflicting pain as long as we do not drag upon their mesenteries, but this does not prove that these receptors are incapable of translating certain types of stimuli into terms of pain.

Hertz believes that the abdominal viscera are exquisitely sensitive to deep pressure stimuli such as those produced by tension. Thus, slight distention of a gut leads to discomfort and marked stretching to severe pain. "The normal stimuli reactions in the intestine are those of contraction and relaxation; these two are

going on continuously. There is, as Meltzer has pointed out, a law of contrary innervation which permits of this wave of contraction and relaxation, and any interference with this law, such as occurs in colic, in obstruction, etc., gives rise to paroxysmal and severe pain. In colic an abnormally strong peristaltic wave occurs in one part of the alimentary canal, the part immediately below which should normally relax, following the law of contrary innervation, is unable to do so, owing to organic disease, or to spasm; the intermediary segment is thus subjected to steadily increasing pressure, which soon produces pain, the distention being an adequate stimulus." (Behan, Pain.) It is difficult to believe that these views of Hertz, Meltzer and others are not correct. As already noted the gastro-intestinal tract, the biliary apparatus, the pancreas, and the spleen are developmentally midline structures, their ultimate anatomical positions being merely due to the exigencies of storage space in the abdomen. The vascular and nerve supply of these structures must correspond with their developmental peculiarities and is essentially midline no matter how much the nerve fibers have been elongated to suit the acquired positions of the viscera. This being so it follows that pain such as may be produced by increased peristalsis must be primarily referred to the midline of the body. Of course after the stimuli have acted long enough or violently enough to produce centers of radiation, *i. e.*, to give rise to viscerosensory reflex phenomena, then the secondary or later pains may appear. One must not ignore the distribution of fibers of the right phrenic nerve to the anterior parietal peritoneum as low down as the umbilicus and their connection with the solar plexus through the phrenic ganglion, etc. A general disturbance of the solar plexus gives rise to certain symptoms common to many affections. A blow on the pit of the stomach may occasion nausea, vomiting, and colicky pains besides shock. Emotion, acting probably through the vagi, may cause nausea, vomiting, and colic. Acute cholecystitis may begin with a sensation of hunger followed by epigastric pain, nausea, and vomiting. All these symptoms are merely evidences of a general solar-plexus disturbance.

Confusion of symptoms may also arise by the intermediation of an axon reflex. "Every sympathetic ganglion is connected with the central nervous system, brain and cord, by efferent spinal fibers, preganglionic fibers, which terminate by arborization around the dendrites of the sympathetic cells. The efferent fibers arising from the latter may be designated postganglionic fibers." Langley and Anderson "give reasons to believe that any one preganglionic fiber may connect by collaterals with several sympathetic cells." (Howell.)

"The preganglionic fibers from which collaterals arise proceed *past* the sympathetic ganglion to arborize around nerve cells located peripherally, *i. e.*, in some viscus. When this viscus is inflamed, etc., an impulse travels (antidromically) up to the cell, thence to

another preganglionic fiber and therefore to ganglionic cells whose axons (postganglionic) are distributed to other viscera. By the disturbances which these impulses thus bring about (local spasms, vascular disturbances) afferent stimuli are set up which proceed to the nerve centers, but the viscus thus affected by the axon reflex may be far removed from that which is the seat of disease." (J. J. MacLeod.)

The complexity of the nerve connections of the viscera, the perfection attained in the fulfilment of their vegetative or automatic functions, and the rarity of the higher centers being given cognizance of what is going on in the digestive tract, apart from a feeling of well being or satisfaction, excuse if they do not explain the confusion in the differential diagnosis of such distinct anatomic entities as appendicitis, pancreatitis, cholecystitis, gastric and duodenal ulcers.

The referred pains of which we have been speaking may be closely simulated by other very important pains. Inflammation extending from the organ primarily involved may of course come into a region supplied by spinal nerves and thus pain result, such as the lumbar pain experienced in cases of retrocecal appendicitis, or the inflammation may spread to another organ adherent to that primarily involved, and thus a secondary referred pain may be noted. An example of this latter condition is where an inflamed appendix becomes adherent to the prostate and gives rise to pain at the point of the penis. In appendicitis pain may be experienced on the left side of the abdomen through direct extension of peritonitis or possibly, in the absence of such extension, by *allochiria*, because, according to Head and Howell, "when from any cause one or other of the cutaneous senses is depressed in a given area stimulation in this region may give sensations which are referred to a symmetrical area on the opposite side of the body."

The nerve supply of the renal pelvis and ureter comes through the inferior mesenteric, spermatic, and hypogastric plexuses, and, according to Head, their central connections are through the tenth, eleventh, and twelfth dorsal and first lumbar nerves.

Unlike the gastro-intestinal canal the kidneys and ureters are paired organs—they are not of midline origin. Pain in the renal pelvis and ureter seems to be excited principally by vigorous contractions of their unstriated muscular fibers; is of the viscerosensory reflex type, and is referred to the area of distribution of the eleventh dorsal to the first or second lumbar. Thus the pain in renal colic begins in the back above the crest of the ilium, passes around in front, and slants down to the testicle. The peculiar course of the pain does not give much information regarding the site of the stone. A stone situated low down in the ureter may cause contractions of the ureteral musculature beginning at the renal pelvis and passing downward—these give rise to the classical pain as described above. In a man of thirty-four years who suffered many attacks of severe pain situated at or below McBurney's point with localized

tenderness, rigidity, and fulness, but without any pain in the epigastrium or umbilicus and without any true nausea, there was pain in the right testicle, but there was no fever. Urinary examination showing blood shadows, a Roentgen-ray examination was made which showed a calculus in the pelvis of the kidney well above any point where pain or tenderness had been experienced. In this case no wave of peristalsis was likely to pass down the ureter. Pressure and percussion over the kidney elicited no symptoms, but pressure over the sensitized abdominal wall near McBurney's point did evoke pain distant from the focus of irritation in the renal pelvis. Mackenzie considers that when attacks of renal colic always begin with pain at one definite spot, no matter how that pain may radiate it is very strong evidence that the calculus is remaining fixed in one position. Should the calculus move downward it is probable that the impulses passing up through the sympathetic will reach lower cord segments, and radiating there will affect nerves with different peripheral distribution.

In some cases of renal colic symptoms of intestinal obstruction may lead to error in diagnosis. These symptoms may perhaps be explained by a consideration of the nerve supply of the anal region. The sympathetic supply to the rectum comes from the inferior mesenteric and the upper and lower divisions of the hypogastric plexuses, while the cerebrospinal supply comes through the second, third, and fourth sacral nerves. "It has been shown by experiments on animals that the cerebrospinal nerves (from the second, third, and fourth sacral) convey motor impulses to the longitudinal fibers but inhibitory impulses to the circular muscular fibers. In like manner the branches from the sympathetic convey motor fibers (derived from some of the lumbar rami communicantes) to the circular muscle, and inhibitory to the longitudinal muscle of the rectum. The reflex centre which governs the action of the sphincters and the muscular fibers of the rectum ("defecation centre") is situated in the lumbar region of the cord." (Cunningham.)

From this it appears possible that impulses passing up from the ureter to the aortic plexuses may produce a disturbance there, sufficient to cause the transmission of motor impulses through the hypogastric plexus to the rectal sphincters and thus set up a tonic contraction. Such tonic contraction is present in the cases where renal colic is mistaken for obstruction.

The urinary bladder is developmentally a midline organ and the pains which result from its irritation are also midline. The nerve supply is from the sympathetic and comes from the upper lumbar region and from the sacral autonomic (second and third sacral). Thus sensory symptoms appear in two regions, viz., in the area of distribution (1) of the upper lumbar nerves, *i. e.*, in the hypogastrium and (2) of some of the sacral nerves, *i. e.*, in the perineum and penis. As the nerve supply of the bladder and of the rectum is in some respects similar it is no wonder that a

patient sometimes is in doubt as to whether certain pelvic sensations are a call for urination or defecation, or for both.

The nerve supply of the prostate and seminal vesicles is derived from the hypogastric plexus. When these organs are the seat of inflammation, especially of a chronic variety, there may be few if any symptoms drawing attention to them. The impulses passing up through the hypogastric plexus may radiate to such an extent that much confusion may result. Hugh Young<sup>1</sup> writes: "The nervous symptoms are often so remote and disconnected that the prostate is not suspected. I have seen many cases of lumbago, sciatica, vague pains in the back, hips, thighs, perineum, groin, and often as far as the soles of the feet, caused by chronic inflammations of the prostate and seminal vesicles which by involving nerve terminals cause stimuli to be sent to the spinal cord and there transmitted to other visceral and superficial regions according to the dicta laid down by Head in his explanation of the etiology of referred pains. I hope that I may be pardoned for digressing somewhat to call attention thus to the great importance of examining the prostate in many painful conditions anywhere between the diaphragm and toes when there are no localizing symptoms to direct attention to the prostate itself. In such cases it is often the site of an extensive chronic inflammatory process which is the cause of the whole trouble. I know of ten cases in which there was operation for renal calculus, the symptoms of which were typical; severe intermittent colicky pain radiating to the groin and associated with symptoms of hematuria and entirely due to a chronic inflammatory process in the prostate and seminal vesicles with reflex referred pains to the kidney region, the blood coming from a congested and inflamed posterior urethra." When one makes a rectal examination in a patient suffering from a number of rather obscure pains and finds exquisite tenderness of the prostate and vesicles, and especially if pressure on the vesicles causes a flow of pus into the urethra, one is very strongly inclined to believe that he has discovered the *fons et origo mali*. It is necessary to remember, however, that in the case of prostatitis and vesiculitis the more or less distant pains may be due to the action of toxins and not to radiation of impulses through the sympathetic.

The object of this paper has been to endeavor to systematize some of our common knowledge and some of our common theories regarding the incidence and distribution of pain produced by disease affecting the abdominal organs supplied by the sympathetic nervous system. In his own work the author has found this rather crude systematization useful and hopes that it may also be of service to others.

<sup>1</sup> Jour. Am. Med. Assn., September 13, 1913.

## ENDOTHELIAL PHAGOCYTES IN PLEURAL EXUDATE DUE TO THE BACILLUS TYPHOSUS.

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THE important part played by phagocytic endothelial cells in the pathology of typhoid fever has been recognized since Mallory,<sup>1</sup> in 1898, after a careful histological study of a large mass of material, came to the conclusion<sup>2</sup> that "the typhoid bacillus produces a mild type of inflammatory reaction consisting almost entirely of endothelial leukocytes which accumulate in large numbers where the typhoid toxin is strongest and thus form the lesions characteristic of typhoid fever. These endothelial leukocytes are strongly phagocytic for other cells, incorporating and digesting large numbers of them. In the intestinal lesions they take up chiefly lymphocytes, in the spleen, red blood-corpuscles, and in the blood-vessels, especially of the portal circulation, polymorphonuclear leukocytes and red blood-corpuscles." These endothelial phagocytes were demonstrable not only in the lymph nodules of the Peyer's patches and of the spleen, but also in the mesenteric lymph nodes, the liver, bone-marrow, clotted blood in the heart and in the alveolar exudate of pneumonia complicating typhoid fever. Mallory, moreover, quotes Eichhorst as having seen similar cells in the blood drawn from the tip of the finger of a typhoid patient during the second week of the disease. In all the localities mentioned the phagocytic cells have the same size and appearance while the engulfed cells vary in type according to the locality. The endothelial phagocytes are uniformly large, with more or less round, lightly staining, eccentrically placed nuclei, and a protoplasm which stains with varying intensity. The formation of phagocytic cells by proliferation from endothelial cells was not claimed by Mallory to be peculiar to typhoid except in regard to location, extent, and degree. He believes that their formation in large numbers may be the result of any mild toxin which acts diffusely and causes proliferation and not necrosis. Under these conditions it is clear that there is a close relationship histologically between tuberculosis and the typhoid process, and this becomes of considerable diagnostic interest when the reactions to infection of a serous surface, such as the pleura, are studied.

The pleura is covered throughout by a single layer of endothelial cells, and these cells appear in small numbers and are readily

<sup>1</sup> Jour. Exp. Med., 1898, iii, 611.

<sup>2</sup> Mallory, F. B., Principles of Pathological Histology, 1914, p. 165.

recognized in stained preparations of the sediment from almost all collections of fluid in the pleural cavity. By some they are referred to as endothelial cells and by others as large mononuclears, and it is claimed that similar forms may arise from connective-tissue cells, from the perivascular lymph spaces, or from the blood stream. They resemble very closely the endothelial phagocytes which proliferate in various localities in typhoid fever.

In mechanical effusions the endothelial cells are seldom numerous, but often occur in groups of two or more. Such groups are spoken of by the French writers as "placards" or plaques, and have long been considered as indicating a mechanical or non-inflammatory effusion. Widal, Ravaut, and Dopter,<sup>3</sup> in 1902, emphasized the fact that in a mechanical effusion the endothelial cells are desquamated in groups and remain joined together and typical in appearance, while in an infectious pleurisy with effusion the endothelial cells may at first be joined in plaques, but they soon separate and then become markedly altered in appearance. Thus they become swollen and stain poorly, vacuoles appear in the protoplasm, and the cell outline becomes indistinct. Also, it is only after the cell masses separate into single cells that they may exhibit phagocytic properties. This, however, is unusual in mechanical effusions. In all pleural effusions due to organisms other than the typhoid or tubercle bacillus the endothelial cells play but a small part and are usually lost sight of in the great polymorphonuclear reaction.

When the tubercle bacillus is the etiological factor the pleural effusion might be expected to show in stained preparations at least a moderate number of endothelial cells and lymphocytes. Some observers, however, claim that while numerous endothelial cells may be present early in a tuberculous effusion, yet once the pleura becomes covered by a fibrinous membrane this variety of cell will cease to be found, and lymphocytes will become the sole or at least the predominating form. As a result of this the finding of endothelial cells in an effusion of some duration has been considered as a strong argument against the effusion being of tuberculous origin, and Naunyn goes so far as to state that the presence of endothelial cells excludes tuberculosis. On the other hand, Koster<sup>4</sup> found endothelial cells in the effusion of almost 50 per cent. of the known cases of tuberculosis he investigated, and other observers corroborate this. In no case, however, has the endothelial cell been described as the predominating form, nor is phagocytosis mentioned.

Typhoid pleurisy is not common (an incidence of about 1 to 2 per cent., in large series of reported cases), and there are but a few records of the cytology of effusion due to this infection. The cases reported indicate considerable variation in the cell picture.

<sup>3</sup> *Compt. rend. d. l. Soc. de biol.*, 1902, liv, 1005.

<sup>4</sup> *Nord. Med. Ark.*, 1905, xxxviii, H. 3, p. 1.



Widal and Ravaut,<sup>5</sup> to whom we owe the first systematic study of cytodiagnosis in puncture fluids, state that typhoid pleurisies are often hemorrhagic and contain a relative abundance of large mononuclear cells. Vincent<sup>6</sup> in each of two cases of pleurisy in typhoid fever, found that the effusion, although purulent, contained a considerable number of endothelial cells. He makes no mention of phagocytosis nor did cultures show the *Bacillus typhosus*; on the other hand, one effusion produced tuberculosis when injected into a guinea-pig. Widal and Lemierre<sup>7</sup> report a case in which endothelial cells predominated in the effusion. Some of these cells were vacuolated and of very large size, but no mention is made of phagocytosis. In this case the effusion yielded the typhoid bacillus on culture and also a positive agglutination test for the typhoid bacillus. The pleural effusion observed by Levi<sup>8</sup> in the course of typhoid fever, was sterile, but contained numerous polymorphonuclear cells and a moderate number of large mononuclears. Phagocytosis is not mentioned. Earl<sup>9</sup> states that the typhoid bacillus calls forth a polymorphonuclear excess of from 50 to 80 per cent. of the cells of an effusion.

The variations in these findings are probably to be explained by the fact that, clinically, typhoid pleurisy appears in two more or less distinct forms, and also that the effusions studied were obtained at different stages of the process. Pleurisy may complicate the onset of typhoid fever, and this is the form which has led to the use of the term pleurotyphoid by the French. The pleuritic symptoms may be marked but little or no effusion develops, and the whole process usually disappears after a few days. On the other hand, pleurisy may develop late in the disease at the time when purulent complications commonly occur. This form goes rapidly on to empyema, and is comparable in every way to the other purulent complications of the disease. The cells in such purulent collections are almost wholly polymorphonuclears, and a pyogenic coccus is sometimes obtained upon culture either alone or with the *Bacillus typhosus*. It is impossible to say whether in these purulent effusions the polymorphonuclear reaction is to be attributed to a greater intensity or concentration of the typhoid toxin or to a super-added pyogenic infection.

In the transitory pleurisies occurring early in the course of typhoid fever the typhoid toxin is apparently not present in any great concentration, and one would expect in view of Mallory's work to find that the cells of the effusion were mostly of endothelial origin. Further, it might be expected that these endothelial cells would show active phagocytosis of other cells in the pleural effusion

<sup>5</sup> Compt. rend. d. l. Soc. de biol., 1900, lii, 648.

<sup>6</sup> Semaine méd., 1903, s. 370.

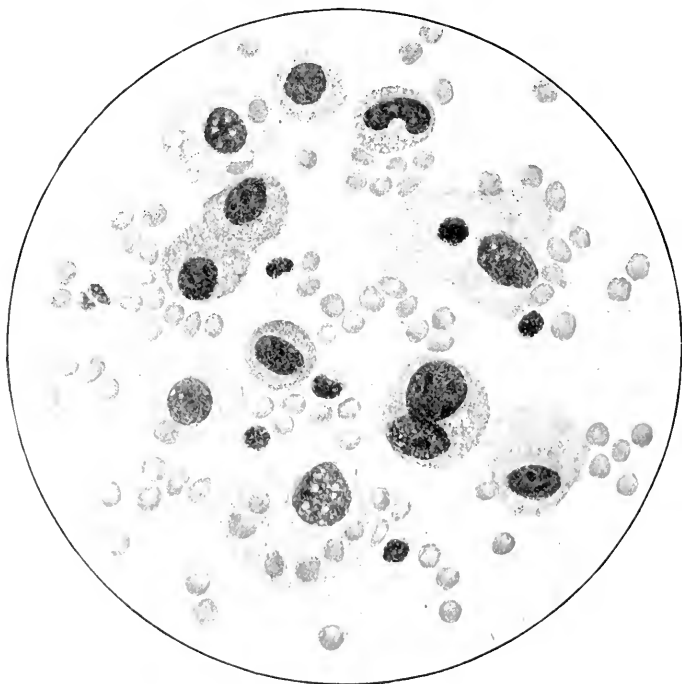
<sup>7</sup> Ibid., 1913, s. 385.

<sup>8</sup> Ibid., 1903, s. 370.

<sup>9</sup> Dublin Jour. Med. Sci., 1903, cxvi, 409.

just as do the endothelial leukocytes arising in other parts of the body in response to the typhoid infection. A careful search of the literature, however, does not reveal any record of such a finding, and the present example of endothelial phagocytosis in pleural exudate due to the *Bacillus typhosus* is therefore reported.

CASE.—The patient, an adult male, with no previous medical history, entered the hospital of the University of Pennsylvania, stating that he had been ill with fever and chills for three weeks. He complained of no localizing symptoms, but upon questioning admitted the presence of a slight pain in the chest for a day or two.



Endothelial phagocytes from pleural effusion due to *Bacillus typhosus*.

The temperature and pulse were elevated. Physical examination revealed nothing abnormal other than the signs of a small effusion at the base of the right lung. Upon aspiration a few cubic centimeters of hemorrhagic serous fluid were withdrawn, and from the cytology of this a diagnosis of pleurisy due to the typhoid bacillus was ventured. This diagnosis was promptly verified by finding that both the blood serum and the effusion gave a positive agglutination test with typhoid bacilli and later by obtaining the *Bacillus typhosus* in pure culture from both the blood and the effusion. The titre of agglutination was 1 to 1000 in the blood, and 1 to 800 in the effusion. A second aspiration several days later gave

similar fluid, but all signs of effusion then disappeared and no fluid was obtained on a third thoracentesis. The patient ran a typical typhoid course, without complications, to complete recovery, and at no time could any evidence of pulmonary disease be found either by physical examination or by stereoscopic roentgenographs.

The fluid obtained by aspiration was distinctly hemorrhagic but did not clot upon standing. Spreads made from the sediment and stained with Wright's stain showed the unusual cytology which is well illustrated in the accompanying drawing of selected cells. Excluding erythrocytes, about 60 per cent. of the cells of the effusion were large mononuclear cells with more or less round nuclei which were usually placed eccentrically and did not stain as deeply as did the nucleus of the small lymphocyte. The protoplasm of these large mononuclear cells varied in appearance; sometimes it was stained uniformly and deeply, while in other instances it was vacuolated and stained palely. In every respect these cells resembled the endothelial leukocytes or macrophages described by Mallory. A moderate number showed phagocytosis and had engulfed one or more erythrocytes. Several had engulfed lymphocytes and one instance of phagocytosis of a polymorphonuclear cell was observed. Some of the cells ingested showed evidence of digestion, while others appeared unaltered. Occasionally the endothelial cells were grouped together in plaques and these cells never showed phagocytosis. Through many gradations these endothelial cells merged into the typical mononuclear of the circulating blood and it was impossible to draw any distinguishing line. The effusion contained these cells in great excess of the white-blood cell count of the circulating blood and a careful search of stained preparations of the latter failed to reveal any large endothelial cells or any phagocytosis by the usual mononuclears.

This observation of the endothelial character of the reaction of the pleura to the typhoid bacillus and of the phagocytic power of such cells in a pleural effusion is of interest not merely from its correlation of typhoid pleurisy to the general pathology of typhoid fever, as described by Mallory, but also from its possible diagnostic significance. In the case here reported the diagnosis was ventured with hesitation, but it would be warranted with greater confidence in the future upon finding a similar cytology. Pleurisy with effusion early in the course of typhoid fever is uncommon, but in any suspicious case an effusion should certainly have its cytology determined, if by this simple step a diagnosis may even occasionally be reached.

**CONCLUSION.** Pleurisy with effusion due to the *Bacillus typhosus* may occur early in the course of typhoid fever. The effusion is apt to be hemorrhagic and to contain a large number of endothelial leukocytes similar to those found elsewhere in the lesions of typhoid fever. These endothelial macrophages show phagocytosis of other cells, especially the erythrocytes of the effusion.

THE PROPHYLACTIC USE OF TETANUS ANTITOXIN.<sup>1</sup>

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IN 1890 Behring and Kitasato published in the *Deutsche medizinische Wochenschrift* an article entitled "Ueber das Zustandekommen der Diphtheria-Immunität und der Tetanus-Immunität bei Thieren." In this paper for the first time are laid down the principles which underlie the elaboration and properties of tetanus antitoxin. The authors showed that when rabbits or mice had been appropriately treated with tetanus toxin of reduced virulence they were not only able to withstand inoculation by fully virulent tetanus bacilli, but were also protected against the injection of twenty times the minimal lethal dose of tetanus toxin. In short, these animals had been vaccinated by means of tetanus toxin and had thereby acquired an active immunity. This immunity was found to rest largely in the blood serum, which when separated from the blood of these animals and injected into other animals was able to afford protection against subsequent injections of otherwise fatal doses of tetanus toxin or the inoculation of virulent tetanus cultures. One produced in these latter animals, by the injection of this antitoxic serum, a passive or so-called prophylactic immunity against tetanus. The evidence that this serum also possesses certain curative possibilities, and can be used as a therapeutic remedy, with more or less success against outbroken tetanus in man and animals, will be discussed in a future paper. At present our attention must be confined not to the cure but to the prevention of tetanus, not to the therapeutic but to the prophylactic properties of tetanus antitoxin.

On the laboratory side the facts in regard to the protective properties of tetanus antitoxin established by Kitasato and Behring were rapidly confirmed and amplified by other workers, among these Tizzoni, Roux and Vaillard, Donitz and Tavel. Thus, Roux and Vaillard stated in 1893 that antitetanic serum injected, even in extremely small doses, before the tetanus toxin would surely prevent tetanus, and Tavel, in 1895, designated the prophylactic inoculation of the serum as "absolutely certain." In fact, so positive and sure did this protective action of antitoxin appear that for nearly a decade clinical and laboratory efforts were almost entirely directed toward establishing the value of tetanus antitoxin as a curative agent and little or no attention was devoted to its acknowledged prophylactic value.

Nocard was the first to emphasize by practical application the usefulness of the serum as a protection against tetanus. The frequency of this disease following operations on horses led him early to test the effect of systematic prophylactic inoculation in all injured or operated animals, and in 1897 he reported some of his results to the French Académie de Médecine. Of 3500 horses inoculated in the preceding twenty-two months the results were known in 2727. Not one of these 2727 horses developed tetanus in spite of the fact that they came from a quarter of Paris where this disease was very prevalent and where in the same length of time 259 cases of tetanus occurred among non-inoculated animals. Of the 2727 horses, 2300 were inoculated immediately following the operation (in most cases castration). Similar results have been reported by other veterinary surgeons, for example, Bigot, Sundt, Rickmann, and Mullotte.

Nandrin, in whose practice, during a course of five years, 8 colts had died of tetanus infection of navel, operation wounds, etc., in the succeeding six years had used preventive injections of antitoxin with entire success. Pecus, after only a single protective inoculation in 1500 horses among which 500 had been wounded by stepping on nails, had not seen a single case of tetanus. The Höchst Farbwerke relate that in the bacteriological division, in which yearly about 300 horses and mules are used to produce serums, since the establishment of systematic and regular prophylactic injections of antitetanic serum, not one case of spontaneous tetanus has been observed. In the United States, McFarland (1903) reported that in a stable of 800 horses the mortality from tetanus became so high that strenuous sanitary measures were demanded. Accordingly the stalls and horses were thoroughly cleansed and disinfected, but without success. The decision to move into entirely new quarters was made when the use of tetanus antitoxin was suggested. The results were most gratifying. The prophylactic injections were first used systematically in 1899, and since that time the yearly mortality from tetanus had remained below 1 per cent. Munich, having successfully protected 48 injured and operated animals, three years later added 150 cases with only one failure. Vaillard, in a report of statistics collected from ten veterinary surgeons, stated that among 13,124 animals which had been injected with antitetanic serum, after either a surgical operation or an injury, not one had developed tetanus. These results led him to recommend strongly that this method should receive more consideration in human medicine.

Before this time, however, the value of prophylaxis against tetanus in human beings was being recognized. As early as 1899 v. Rosthorn reported that in his obstetric service in Prag he was disturbed by an epidemic of tetanus. Almost every woman who was delivered became infected and died. No source could be found.

and in spite of "most thorough disinfection," with closure of the clinic at two different periods, no relief was obtained until antitoxin injections were systematically used. "We possess in tetanus antitoxin an agent that not only is able to permit a favorable prognosis in the ordinary uncomplicated case of traumatic tetanus, but also can prevent the further spread of an epidemic of puerperal tetanus, which disease may occur even after the most careful asepsis." (v. Rosthorn.)

The following year (1900) v. Leyden and Blumenthal, impressed by Nocard's results as well as those of their own experiments, wrote: "The employment of prophylactic antitetanic serum is to be recommended for all suspicious cases of abortion or of injuries, especially those in which dirt has entered."

Herhold, in 1901, described four cases of tetanus which occurred within a period of eight weeks in a field hospital in China. After systematic antitoxin injections in all cases with unclean wounds no further tetanus appeared. Schwartz in the same year declared that his hospital in Cochin, China, had become a regular "breeding-place" for tetanus until antitoxin finally ended the epidemic.

At the Fifteenth French Congress of Surgery, in 1902, there were especially favorable results reported from the systematic prophylactic treatment of all suspicious wounds. Championnière, when a case of puerperal tetanus on his service had been shortly followed by two other cases which developed in spite of every precaution, on the advice of Roux administered prophylactic antitoxin to all subsequent confinement cases, and for the past four years had encountered no further trouble from tetanus. Raboul, Bazy, Guinard, and Schwartz declared that for years routine prophylactic injections of serum in all cases with unclean wounds had been a rule on their services, and in no case so treated had tetanus developed. The first three surgeons each observed a case of tetanus in which the prophylactic injection had been accidentally omitted. Vallas went so far as to insist that for a physician not to give prophylactic antitoxin to all cases with dirty wounds was a failure in correct treatment. He believed the universal practice of this method would cause tetanus to disappear.

In this year also Barthélemy, from the results of experiments on animals, strongly recommended the intravenous administration of antitoxin for prophylactic purposes, and predicted that by this method many lives might be saved even when the antitoxin was administered late in the incubation period.

Calmette, in 1903, proposed a new method of using antitoxin on wounds, namely, as a dry powder. In experiments on tetanus-infected wounds in guinea-pigs he was able to prevent death by using antitoxin in this manner as late as seven hours after infection. As a result of these experiments and his experiences on the west coast of Africa, where wounds were generally unclean and tetanus

extremely prevalent, he advised in all cases of injuries prophylactic inoculation either by subcutaneous injection of 10 c.c. fluid serum or by the application of dry antitoxin on the wound. He especially recommended the sprinkling of powdered antitoxin on the umbilical cord stumps of infants for combating tetanus neonatorum. That in such cases the method has real value was shown by Letulle, who used it extensively in Indo-China, where one-fifth of the newborn babies died of tetanus. After the systematic use of the antitoxin powder tetanus neonatorum practically disappeared. Norris in this same year, from a study of 57 cases, concluded that all those with wounds in which there might be a possibility of tetanus infection should receive prophylactic injections of antitoxin.

In 1905 Suter gave a very thorough review of this subject with statistics from Julliard's surgical clinic in the Geneva Hospital, where, since 1896, more than 700 patients with fresh wounds had received prophylactic injections of tetanus antitoxin (10 c.c.). Two patients in whom the treatment was accidentally omitted developed tetanus and died, while only one of the 700 treated cases showed any symptoms of the disease and no bad results followed in consequence of the serum injections, except for a light urticarial eruption in two cases.

At the Thirty-fifth Congress of the German Surgical Association, held in Berlin in 1906, the subject of tetanus prophylaxis was vigorously discussed. The opinions there expressed were decidedly varying; for example, Zoëge v. Manteuffel, Wreden, Körte, and others opposed as useless the administration of tetanus antitoxic serum, while Freiderick, Hecker, Kocher, Pochhammer, and Uhlenhuth expressed their confidence in the method. Kocher declared: "I should strongly resent it and call him to account if a doctor, in treating a relative of mine who had received a wound which was infected with street dirt, did not administer a prophylactic injection of tetanus antitoxin." Uhlenhuth, after reporting on the frequency of the tetanus spores in the clothing of soldiers, added that all soldiers of the II Army Corps whose wounds were complicated by earth, filth, or pieces of clothing were ordered to receive an immunizing dose of antitetanic serum.

Lotheissen, in this same year, after a thorough study of the subject, concluded that tetanus antitoxin was of far greater value as a prophylactic than as a cure. He described the case of a sixty-year-old tanner who after a severe injury of the right forearm showed suppuration of the wound. In the secretions of this wound were found, by bacteriological examination, tetanus bacilli, and, accordingly, on the seventh day after injury he was given 100 units of tetanus antitoxin. No symptoms of tetanus developed at any time. Similar findings have been reported by Kolb and Laubenheimer. However, such facts cannot be regarded as sure proofs

for the efficacy of antitoxin, as, among others, Bain has demonstrated the presence of tetanus bacilli in wounds where the disease did not develop and no antitoxin was given.

After tabulating the unfavorable results seen up to 1906 in the preventive treatment of tetanus, Bär stated that the most careful antiseptic treatment of complicated fractures into which dirt had entered was not able to render harmless the bacteria which might be buried in the wound, especially in those injuries produced by fragments of exploding shells where, because of the infected pieces burying themselves in the body, the danger of tetanus was more pronounced. He concluded from the reports of Herhold and Hohlbeck that, in the Russian-Japanese war, serum prophylaxis had been used with success.

A second article from Suter, in 1907, extensively considered all the phases of tetanus prevention. He stated that diligent search of the literature had failed to show a case where antitoxin had done harm, and disagreed with von Manteuffel, who thought that prophylaxis was impracticable in war. Suter admitted, however, that antitoxin in its present form might be difficult to use on the front—nevertheless, if given early enough, many deaths from tetanus might be prevented, a view shared by Manning, who declared: "Preventive inoculation is, up to the present time, the best means of lowering the mortality of tetanus."

In the following year Le Deutu appeared as a strong partisan of prophylaxis, advising large and repeated doses of serum. He thought that every one of the 1200 deaths from tetanus occurring in the Franco-Prussian war of 1870 could have been prevented by antitoxin. Lucas-Championnière and also Vaillard defended the efficacy of preventive inoculation in spite of the increasing reports of failures following its use, especially in France.

Grazer, in 1910, recommended treating all wounds suspected of tetanus infection with the prophylactic injection of 20 to 100 units of antitoxin, and in the following year Remertz gave his opinion that this treatment would reduce the death rate of tetanus one-half, and that it should always be employed in wounds of both men and horses when such wounds were received in regions where tetanus was known to be prevalent. In this year also Biron and Pied confessed that, doubting its efficacy, they had not used prophylactic antitoxin from 1895 to 1902, and during that period had met with 11 cases of tetanus. From 1905 to 1910 the serum was used as routine treatment and no tetanus had appeared. Tizzoni, in 1912, introduced the theory that the blood of normal individuals to a certain extent would neutralize tetanus toxin, but with the help of antitoxin an enormous temporary increase in immunity could be obtained. For this reason he emphasized the value of prophylaxis, and recommended its use in surgical operations and after all shot wounds.



One of the most impressive series of facts in relation to the prevention of tetanus is associated with the annual Fourth of July celebration in the United States. For many years this holiday had been accompanied by an increasing number of both minor and major injuries, caused by blank cartridges, cannon crackers, toy pistols, etc. A considerable proportion of these injuries, nearly 10 per cent., were followed by tetanus, usually of a very virulent type. Thus in 1900, 500 deaths were said to have been due to tetanus, directly caused by wounds received during this celebration. Hence the *Journal of the American Medical Association* began in 1903 the collection of careful statistics and also at the same time conducted an extensive campaign both to discourage the use of toy pistols and similar injury producers and to encourage the treatment with tetanus antitoxin of all injured persons. The results of this campaign may be seen from the accompanying table, which shows that in 1904 the effect became first apparent, at which time a sudden drop occurred from 415 cases of tetanus (or 9.35 per cent.) of all injured persons in 1903 to 111 (or 2.52 per cent.) in the following year.

TABLE 1.<sup>1</sup>

Year.	Total injured.	Tetanus cases.	Per cent. of tetanus cases.	Deaths from tetanus.	Tetanus mortality. per cent.
1903	4449	415	9.35	406	97.8
1904	4169	111	2.52	87	78.4
1905	5176	104	2.01	87	84.0
1906	5466	89	1.45	75	84.0
1907	4413	73	1.65	62	84.0
1908	5623	76	1.35	55	72.4
1909	5307	150	2.82	125	83.2
1910	2923	72	2.46	67	93.0
1911	1603	18	1.12	10	55.5
1912	988	7	0.71	6	86.0
1913	1163	4	0.35	3	75.0
1914	1506	3	0.2	3	100.0

In respect to the use of antitoxin the *Journal* of that year (1904) gave the following comment: "The prophylactic treatment of all blank cartridge, giant cracker, and other similar wounds of the Fourth of July has been demonstrated to be positively successful many times before, but probably never on so large a scale as this year—having been employed in more cases than ever before. We have now records of upward of one thousand administrations of antitoxin in this way without a single untoward result of any importance and without a single case of tetanus developing. What motive can there be, therefore, in treating a Fourth of July injury without the prophylactic injection?" Individual reports have only added to the impressiveness of these statements. For example, in St. Louis, in 1903, according to Scherck, 56 cases of Fourth of July injuries occurred, from which 16 fatal cases of tetanus developed.

<sup>1</sup> Fourth of July injuries and tetanus, from statistics collected by Jour. Amer. Med. Assn.

In the three years following, 36, 84, and 170 such wounds, under prophylactic treatment, showed no case of tetanus. In the Harlem Hospital 100 cases of gunshot wounds were treated with antitoxin and no tetanus appeared. Luckett injected 60 of these injuries, each with 10 c.c. antitoxin, with the same success. However, one other case of his, a woman, who was treated with dry powdered antitoxin because she objected to the subcutaneous injection, later succumbed to a fatal attack of tetanus.

Nevertheless the judgment of the clinical world is not so unanimous as the foregoing might lead one to believe. In both France and Germany there is a consistent minority of physicians who point to the fact that ever since tetanus antitoxin has been used prophylactically there have appeared occasional cases of tetanus which have developed in spite of the treatment, *i. e.*, in a small but definite percentage of all cases so treated, the method had failed to give adequate protection. These failures have been especially numerous in Germany in the present war, and have led to a feeling of pessimistic skepticism in the minds of many doctors toward the use of tetanus antitoxin for any purpose whatsoever.

Accordingly it is proposed here to classify and analyze in two groups (1) the theoretical considerations and (2) the actual facts that underlie these cases, with the purpose of determining, if possible, the reasons for the failures and of establishing more firmly the principles which should govern the prophylactic administration of tetanus antitoxin. In group 1, as one of the most important of the theoretical considerations, may be mentioned the abnormal reactions exhibited by some individuals (1) toward certain diseases and (2) toward foreign serums. In the first class one finds those variations from the normal average which are well recognized in both men and animals. These individuals show such an extreme sensitiveness to certain toxins that the general rules for prevention and cure may prove entirely inadequate. So in tetanus the conditions for the growth of the bacillus may be so favorable, the absorption of the toxin so rapid and complete, and the sensitiveness of the vital centres to this toxin so exaggerated, that extraordinary and unexpected intoxication occurs in spite of the usual prophylactic and therapeutic measures. In the second class there is an abnormal reaction toward the serum itself. As far as can be determined the antitoxic property is added to the blood serum without appreciably affecting its physical or chemical constituents, and, aside from its ability to neutralize tetanus toxin, its fate in the body exactly corresponds to that of any other foreign serum injected under the same conditions. In other words the body endeavors to destroy or eliminate antitoxin just as it does plain horse serum. The elimination is accomplished by the glandular excretory organs, and the destruction supposedly by ferments usually newly formed in the body in response to the irritation of

the presence of this foreign proteid. We shall return to this subject in the discussion of anaphylaxis. Here it is sufficient to indicate the possibility that these ferments may be already present in the body at the time of the first injection in sufficient strength to destroy rapidly and render useless the antitoxic serum that is introduced. In this connection may be noted the fact that the second dose of antitoxin does not give so long a duration of protection as the first. (Behring.) The body has learned, *i. e.*, adapted itself, to destroy more rapidly and efficiently this injected serum. But if this ability by some chance were already possessed by the body cells and fluids before the first injection of the tetanus antitoxin (perhaps because of some previous serum injection), then such an injection might prove not only useless, but under certain circumstances, as will be shown, actually dangerous.

As the second factor in this first group may be considered the question of passive against active immunization. As yet no attempts have been made to provoke active immunity against tetanus in human beings. The dangers associated with tetanus toxin and the efficacy of early administration of tetanus antitoxin have not as yet justified the attempt to protect people against tetanus as against smallpox, typhoid fever, or cholera, *i. e.*, by vaccination. The advantages of active immunity, however, are clear. In the first place the protection is more enduring, usually lasting months or years instead of days, and in the second place, when infection occurs, "protection" is already present and able at once to neutralize the first toxin that may be produced. Also in active immunity foreign serums do not enter into consideration. The protective qualities are then a distinctive property of the body's own cells and fluids. If human serum could be used for antitoxin in human beings it would undoubtedly possess greater value both prophylactically and therapeutically. In fact, Wiedemann reported the case of a child suffering from traumatic tetanus in whom he used the serum obtained from 100 c.c. of the blood of a boy who had recovered from tetanus two years before. Ransom and Kitashima, in Behring's laboratory, found that goats' antitoxin given to other goats produced a passive immunization which was of nearly the same duration as the active immunization of the original goats. Naturally the extensive use of homologous serum in human beings is at present out of the question.

A further and important reason for the adoption of a rational and safe method of active immunization in tetanus is war. Wounded soldiers are notoriously liable to tetanus. The first treatments are often difficult, inadequate, and delayed. Were such soldiers previously actively immunized against tetanus as well as typhoid and cholera a percentage of deaths, always large enough to be disturbing and often extreme, would be almost entirely avoided and the trouble associated with ordinary prophylaxis would be unneces-

sary. Such protection is theoretically entirely possible. A practical and absolutely safe method is alone lacking. Manifestly the methods used at present in animals are not applicable to man, but I am convinced that the question deserves earnest consideration, especially in the light of the lessons learned from the present war. In this connection, Piorkowski has recently proposed the use of a preparation of heated dried cultures of tetanus bacilli which as a powder could confer immunity upon and also save mice when administered with or even later than inoculated garden earth.

The second main group of reasons for failures includes the study of individual cases and the actual circumstances under which failures in these cases have occurred. Accordingly in Table II have been collected and tabulated those cases which could be found in the literature in which prophylaxis failed to afford adequate protection. Similar cases which have occurred in the present war will be reserved for separate consideration.

The first and most important cause of these failures is undoubtedly the rapid formation and absorption of tetanus toxin following the injury. Kitasato inoculated the tails of mice with tetanus cultures and at varying intervals of time cut off the inoculated portions, thereby removing completely all further source of toxin production. He found that one hour after the inoculation such an operation was too late to save the animal from a fatal attack of tetanus. In close association with this fact is the extreme rapidity with which the absorbed toxin is bound to the nerve cells, where it cannot be neutralized. Donitz determined the amount of antitoxin necessary to neutralize a definite quantity of toxin when both were mixed *in vitro*. He then injected this amount of toxin into one ear vein of a series of rabbits, and at varying intervals injected antitoxin into the vein of the opposite ear. In four minutes it was necessary to use two times and in fifteen minutes twenty times the amount of antitoxin which had sufficed *in vitro*, and after one hour forty times this dose could barely save the life of the animal, while at the end of twenty-four hours an enormous increase (3600 doses) did not avail. Donitz concluded, among other things, that in cases of severe poisoning at least the lethal dose of toxin was already combined with the nerve structures at the end of four to eight minutes.<sup>2</sup>

Further evidence of this rapid binding power is presented by Hutchings, who infected the tails of sheep with tetanus cultures, and as soon as symptoms appeared cut off the infected portion. Tests of the blood at this time showed that 2 c.c. contained enough tetanus toxin to kill a 350-gram guinea-pig; 4500 units of anti-

<sup>2</sup> Another conclusion which was drawn by Donitz from these experiments was that "this combined toxin could be again separated from the nerve tissue, neutralized, and rendered harmless by the action of tetanus antitoxin." This conclusion has not been confirmed.

TABLE II.—Showing published cases in which prophylactic applications of tetanus antitoxin failed to prevent tetanus. 0 = recovery; + = death.

No.	Author.	Age.	Interval between injury and injection.	Quantity of serum.	Incubation time, days.	Result.	Remarks.
1	Buschke	?	6 days	5 c.c.	11	1	Author himself doubtful over diagnosis; antitoxin late.
2	Tizzoni	?	4 days	4 gm.	4	0	Antitoxin late.
3	Tizzoni	?	24 hours	?	12	0	Tizzoni serum.
4	Remy	49	Same day	10 c.c.	47	+	"Delayed tetanus."
5	Reclus	25	Same day	7 c.c.	12	+	Intracerebral antitoxin; French serum.
6	Bougle-Reynier	48	Same day	10 c.c.	15	0	"Prolonged incubation."
7	Peyrot	?	?	?	12	+	Details wanting
8	Haltenhoff	3	2½ days	10 c.c.	4½	0	Antitoxin too late; diagnosis in doubt.
9	Ulrich	43	3 days	?	76	0	Delayed tetanus.
10	Maunoury	30	Same day	10 c.c.	26	+	Delayed tetanus.
11	Mauclore	?	1 day	10 c.c.	17	0	Prolonged incubation.
12	Krafft	31	64 hours	10 c.c.	6½	+	Antitoxin too late; intracerebral injections.
13	Vidal	7	1½ hours	15 c.c.	3	+	French serum.
14	Grenda	?	Same day	10 c.c.	5	+	Swiss serum.
15	Lannelongue	?	3 days	10 c.c.	59	+	Delayed tetanus.
16	Tixier	?	5 days	10 c.c.	8	+	Antitoxin too late.
17	Terrier	57	Same day	10 c.c.	87	0	Delayed tetanus.
18	du Sejour	60	1 day	10 c.c.	23	+	Prolonged incubation.
19	Ruter	30	Same day	10 c.c.	47	0	Delayed tetanus.
20	Küster	36	2½ hours	40 A. E.	7	0	German serum.
21	Pochhammer	32	14 hours	20 A. E.	14	+	Antitoxin late; German antitoxin.
22	Kocher	?	?	10 c.c.	21	0	Prolonged incubation.
23	Lotheissen	46	2 days	100 A. E.	6	0	Antitoxin too late.
24	Lop	?	1 hour	?	7	+	Powdered antitoxin.
25	Ochsner	?	16 hours	10 c.c.	12	0	Antitoxin late; French serum.
26	Bell, J.	9	1 day	5 c.c.	47	+	Delayed tetanus.
27	Freeman	?	Same day	10 c.c.	6	0	American serum.
28	McArthur	?	Same day	10 c.c.	14	0	Fractured skull; American serum.
29	Tyson	48	4 days	30 c.c.	12	0	Antitoxin late.
30	Brawan	14	3 days	10 c.c.	4	0	Antitoxin late.
31	Bär	13½	3½ hours	10 c.c.	8	0	Swiss serum.
32	Ellbogen	?	1 day	20 c.c.	18	0	Prolonged incubation.
33	Reynier	20	Same day	10 c.c.	11	0	French serum.
34	Thiery	?	?	10 c.c.	8	+	Essential details lacking.
35	Senecchal	26	6 hours	10 c.c.	8	0	French serum.
36	Mauclaire	34	Same day	?	6	+	French serum.
37	Terrier et Mercedé	18	Same day	10 c.c.	6	+	French serum.
38	Mignard	?	4 hours	?	4	+	French serum.
39	Lang	?	2 days	10 c.c.	11	0	Antitoxin late.
40	Lang	3½	4 hours	10 c.c.	12	+	Swiss serum.
41	Lang	9	2 days	100 A. E.	4	+	Antitoxin late.
42	Luckett	?	?	?	8	+	Powdered antitoxin.
43	Roger	?	?	?	5	+	Powdered antitoxin.
44	Roger	?	?	?	5	+	Powdered antitoxin.
45	Monod et Vanverts	52	Same day	10 c.c.	75	0	Delayed tetanus.
46	Viscontini	40	?	10 c.c.	9	+	Essential details lacking.
47	Vennat et Michelean	?	1 day	10 c.c.	14	+	Diagnosis doubtful.
48	Vennet et Michelean	?	?	10 c.c.	?	0	Diagnosis doubtful.
49	Tuffier	?	3 hours	?	6	+	French serum.
50	Reynier	?	Same day	?	5	+	Powdered antitoxin.
51	Reynier	?	Same day	?	8	+	Powdered antitoxin.
52	Reynier	?	3 hours	?	?	+	Details insufficient.
53	Massol	?	?	?	51	?	Delayed tetanus.
54	d'Hotel	?	Same day	10 c.c.	16	0	Prolonged incubation.
55	van Hayre	19	3 hours	20 c.c.	11	+	Swiss serum.
56	Simon	5	Same day	20 A. E.	?	0	Diagnosis doubtful.
57	Schlatter-Bär	20	3 hours	10 c.c.	23	+	Prolonged incubation.
58	Bär	5	Same day	10 c.c.	21	0	Prolonged incubation.
59	Viscontini	40	?	10 c.c.	10	+	Essential details lacking.
60	Rowan	37	5 hours	1500 units	26	+	Delayed tetanus.
61	Delbet	?	?	?	3 or 4	0	Essential details lacking.
62	Arrou	13	Second day	10 c.c.	8	+	Antitoxin late.
63	Huber	?	?	10 c.c.	6	+	Diagnosis doubtful.
64	Riche	9	10 hours	10 c.c.	8	0	French serum.
65	Potherat	58	Second day	10 c.c.	4	+	Antitoxin late.
66	Ritter	?	?	?	?	+	Insufficient details.

toxin<sup>3</sup> was then injected, and twenty-four hours later a test of the blood showed no toxin present. However, in spite of daily injections of 4500 units the sheep invariably died. Neither the symptoms nor the course of the disease were influenced by these injections.

Many facts lead one to believe that in man we have to deal with nerve structures extremely sensitive to tetanus toxin. Some of the clearest evidence having a bearing on this point occurred in an outbreak of tetanus in St. Louis following the administration of diphtheria antitoxin. Investigation showed that a certain supply of this antitoxin had, in some unknown manner, become contaminated by tetanus toxin (not tetanus spores). A comparison of the amounts of this fluid which had produced accidental death in human beings and the amount found necessary to kill a 300-gram guinea-pig demonstrated that the susceptibility of the two was nearly the same, *e. g.*, 0.1 c.c. would kill a 300-gram guinea-pig, and 10 c.c. was sufficient to produce fatal tetanus in a child weighing fifty pounds. Also the occurrence of symptoms of undoubted tetanus only three and four days—in fact even two days—after the injury indicates the exceeding rapidity with which all these processes may take place.

The second cause for failure in these cases is supplementary to the first and rests in the slowness with which antitoxin is absorbed into the blood stream. In a series of careful experiments Knorr found that in animals subcutaneous antitoxin did not attain its maximum in the blood stream until twenty-four to forty hours had elapsed after the injections. Naturally this time may vary within wide limits, depending upon special conditions. For example, tissues of the young absorb more rapidly than those of the old, the muscles better than the subcutaneous fascias, and these in turn better than the skin. Finally, inflammation, shock, vascular spasm, congestion, heart weakness, etc., all tend to decrease the rate at which antitoxin enters the blood stream. While many of these factors may also operate to decrease the rate of absorption of the toxin it must be remembered that toxin is by its nature readily absorbable, while antitoxin, on the contrary, perhaps because of the larger size of its molecule, is naturally slowly absorbable. From the foregoing it becomes clear that, given a case where toxin is formed and absorbed with unusual rapidity and the antitoxin is injected too late or for some other reasons is absorbed too slowly to neutralize this toxin, harmful and even fatal consequences may readily follow. That such a set of circumstances may occur can be plainly seen from the statistics presented in Table II. The time of giving the antitoxin varied from a few hours to as late

<sup>3</sup> The United States antitoxin unit represents that amount of antitoxin which can save the life of a 350-gram guinea-pig for ninety-six hours when the animal has also received 100 times the minimal lethal dose of a test toxin preserved in the laboratory of the United States Public Health and Marine Hospital Service.

as six days after the injury. Under certain circumstances, as has been demonstrated, a few hours' difference in time might represent the difference between a non-fatal and a fatal intoxication.

The third cause for failures which appears in this table is the short duration of the immunity conferred by injections of antitoxin. Behring stated that the first dose of antitoxin gave an immunity lasting twenty days and that a second injection at the end of this time would add only a further protection of from five to eight days, *i. e.*, repeating the injection diminished the duration of the protective action to five to eight days. According to Tizzoni, antitoxin protects for fourteen days; Delbet estimated the duration at ten days, while Glasser suggested a repetition at the end of eight days and Vaillard declared that the serum ceased to be effective after a week or at the very longest at the end of two weeks. Ruediger in guinea-pigs found that passive immunity against tetanus produced by moderate doses of tetanus antitoxin lasted a little less than three weeks, and that the immunity conferred by larger doses continued only a few days longer. This subject was considered worthy of further experimental proof, and, accordingly, through the kindness of the attending physicians in the Freiburg military hospitals, especially of Prof. Kähler and Dr. Weidenmüller, samples of blood from various patients who had been given prophylactic injections of twenty antitoxin units (German standard) were tested for their antitoxin content.

In these experiments 1 c.c. of the blood serum from these samples was mixed with two or three times the minimal lethal dose of tetanus toxin, and this mixture was injected into the hind leg of rats. The rats varied in weight from 100 to 200 grams and the dose necessary to kill the larger rats was used as the minimal lethal dose. In every case controls were injected with the toxin alone. Other controls were injected with normal blood alone and others with normal blood plus twice the usual minimal lethal dose of toxin. The blood serum alone proved to be non-toxic and neither did it possess any appreciable antitoxic properties. In this particular I was unable to confirm Tizzoni's assertion that the blood of normal persons would neutralize tetanus toxin. In all seventeen samples of human blood were tested. These were removed at intervals of from three to twenty days after the antitoxin injection. All the samples representing a duration below fifteen days held sufficient antitoxin to protect fully the injected animals. Of those taken on the fifteenth day from five samples tested, one rat died from tetanus, the death, however, being delayed three days beyond that of the control. That the other fifteen-day samples held only a diminished amount of antitoxin was shown when after injecting one sample from which only 0.5 c.c. of serum could be obtained death occurred, and in another where the toxin was repeated without

the serum the animal died two days after the control. In a twenty-day sample the rat died one and a half days later than the rat injected with toxin alone. These facts permit the conclusion that passive immunity in man conferred by twenty units of antitoxin is effective for about twelve days and contains some protective powers for eight to ten days longer.

Hence, given a case in which prophylactic antitoxin is administered and for one reason or another the tetanus toxin is not formed or possibly not absorbed until after twelve to fifteen days have passed we may expect very little protection from the antitoxin first given and at the end of twenty-five days absolutely no protection at all.

Consulting again Table II, one finds that in 10 cases from twenty-six to eighty-seven days passed between the last injection of tetanus antitoxin and the first symptoms of tetanus, which here represent examples of what I have called delayed tetanus, and in 8 other cases from fifteen to twenty-three days elapsed (examples of prolonged incubation<sup>4</sup>). In the first group 5 cases died, 4 recovered, and the outcome of 1 is unknown; while in the second group only 2 died and 6 recovered, suggesting that in the latter group the protective effects of the serum had not entirely disappeared.

Examples of a long incubation time in tetanus (delayed tetanus) are of frequent occurrence in the literature, and the possibility of a tetanus infection lying dormant in the body and only developing when favorable circumstances present themselves has been shown in animal experiments. For example, Vaillard and Rouget described instances where guinea-pigs were inoculated with tetanus spores plus lactic acid, and did not develop tetanus until more than four months had elapsed. Such cases of delayed tetanus, as well as those of unduly prolonged incubation, present a problem in both the prophylaxis and the treatment of tetanus which has not yet been satisfactorily solved. Repetitions of the antitoxic serum are not always practical, and, moreover, the succeeding doses always afford an ever-diminishing period of protection. Here, again, the production of active immunity would be of decided advantage.

As the fourth cause for failures may be considered the method of application of the antitoxin, Calmette's recommendation that dry powdered antitoxin be applied locally to the wound led to its widespread use not only in France but also in other parts of Europe and in America. Practically the method has many obvious advantages; theoretically, however, it is not based on logical grounds. First it does not, as a rule, reach the tetanus inciter, the bacilli being buried deep in the tissues. Experience has again and again demonstrated that local disinfection and cleansing are not able to prevent tetanus. Hence for the efficacy of the powder we are largely

<sup>4</sup> The limits for this latter class have been arbitrarily placed at between fifteen and twenty-five days.



dependent on its solution and absorption by the body juices. Under the circumstances not only is this absorption slower than with the fluid antitoxin but manifestly less dependable. Letulle's enthusiasm for its use on the umbilical cords of newborn children may be explained by the fact that in infants absorption by the tissues is extremely rapid, and a fresh wound without inflammatory reaction is much more suited for these applications than a wound filled with blood clots and inflammatory débris, such as is usually presented in adults. Clinical opinions, however, have varied widely. Delbet believed the convenience of the powder was its only recommendation, and that in most cases it was useless. Remertz concluded: "Das bestreuen der Wunde mit Antitoxin in Pulverform ist als nutzlos zu verwerfen." Examination of the cases in Table II tends to confirm this last view. Six cases were treated prophylactically by powdered antitoxin and all six ended in fatal tetanus.

Yet a successful method of local application of antitoxin is demanded. In the well-ordered hospital or physician's office the subcutaneous or even the intravenous injections of antitoxin offer little difficulty. On the other hand, in injured persons far removed from either of these places, especially in those wounded in war, such injections may be very difficult, and while eventually an injured soldier can obtain an injection of antitoxin, in the meantime valuable time may have been lost and a fatal case of tetanus may have been permitted to develop because the antitoxin could not be early enough administered.

Various solutions of this problem have been offered. As early as 1900 Behring stated that experiments on animals had demonstrated the importance of the direct contact of tetanus antitoxin with the infected and toxin-containing tissues, and laid great stress on the advantages of direct application to the point of infection and its vicinity. The results given above show, however, the futility of powder. Behring's general suggestion was applied more successfully by Suter, who soaked tampons with antitoxin and bound these directly to the wound. Bockenheimer proposed mixing antitoxin with salve. Among others, Graser reported good success with the tampons but was unable to obtain results with the salve. Bockenheimer himself did not present convincing proof of the efficacy of this method. His advocacy of the salve was based on the principle that fatty substances possess a certain neutralizing property against tetanus toxin, a fact which led him to recommend, for example, Peruvian balsam salve with or without antitoxin. He also admitted that antitoxin mixed with salves rapidly lost its power to neutralize toxin, and therefore had always to be made freshly. I attempted to immunize rats with a mixture of antitoxin and lanolin by thoroughly rubbing this on the skin. In two separate sets of experiments the treated rats died at the same time as the controls.

Suter's proposal to use liquid antitoxin has this advantage over the powder, namely, it does not need to be first dissolved and therefore more readily penetrates to the deeper tissues of the wound and more quickly mixes with the wound fluids, not only thereby destroying local toxin but also furnishing general protection by absorption into the blood. In my experiments wounds were made in the skin and muscles of the backs of laboratory animals and antitoxin-soaked tampons were bound onto the wounds. Twenty-four hours later the animals were given three times the minimal lethal dose of tetanus toxin and showed no symptoms of tetanus at any time.

This method, however, is wasteful and involves the use of bottles of fluid antitoxin which are not only liable to breakage but also to spontaneous deterioration of the antitoxic properties of the serum. Consequently an attempt was made to combine the advantages of Calmette's method with those of Suter's. Liquid antitoxin was poured on pads of sterile absorbent cotton in such amounts as to render the cotton uniformly moist but not wet enough to drip. These pads were then dried for twenty-four hours in a moderate heat ( $40^{\circ}$  to  $45^{\circ}$  C.). A previously sterilized evaporating dish or earthenware mortar covered with a double layer of filter paper was found satisfactory as a container. Drying in vacuum did not appear to offer any advantages. The dried antitoxin cotton became a stiffened mass, resembling dried paper pulp. This was weighed and then divided into pieces which by weight would represent definite quantities of antitoxin, *e. g.*, if the entire mass contained twenty units of dried antitoxin, one-twentieth by weight would represent one unit. Pieces of this prepared cotton, representing amounts varying from one to two and a half units of antitoxin were then bound on freshly made wounds of rats. The results were not entirely satisfactory. If fresh serum or blood were present in the wound and the dry cotton could be bound closely to the wound, varying degrees of protection were afforded; but more often from lack of fluids no solution of the antitoxin took place and hence no absorption. This latter fact was demonstrated by the following occurrence: The dried cotton was removed from a rat which had succumbed to tetanus in spite of its presence, and after moistening this cotton it was applied to a fresh wound in another rat. A three-times minimal lethal dose of tetanus toxin injected on the following day failed to produce tetanus and the rat remained alive.

This led me to adopt the method of simply keeping the prepared cotton in a sterile container and, when it was required for use, to moisten it with physiological salt solution, distilled water, sterile bouillon, or any clean fluid which might be at hand. To test its efficacy on natural tetanus infections, 10 mice were inoculated with garden earth which in previous experiments had produced tetanus in mice with 100 per cent. mortality; 5 mice received, at the same time with the earth, fragments of dried antitoxin cotton

which had been moistened directly before application to the wound. The other 5 mice, serving as controls, were inoculated with the earth alone and all died from typical tetanus in the course of three days. Of the 5 treated mice 1 only, which had early torn the cotton dressing from the wound, showed any sign of tetanus, and even then it lived for eight days, evidently having received some protection, as it lived five days beyond the controls. The remaining four at no time showed any sign of tetanus. Portions of the prepared cotton tampons were used after they had been kept six weeks, and with these pieces the lives of rats were protected against a three-times minimal lethal dose of tetanus toxin. All the rats treated in this manner have received protection. Each time the cotton was moistened immediately before application to the wound. In two animals which had torn the tampon away shortly after the operation a local tetanus developed, but the rats lived and the local symptoms gradually disappeared.

In this method I believe that the advantages of the powdered antitoxin of Calmette and of the fresh antitoxin tampons of Suter have been retained and the disadvantages removed. I do not wish to be understood as recommending this method as a substitute for the subcutaneous or intravenous injections of fresh potent antitoxin. Where, however, such injections are impracticable these dried antitoxin tampons which hold their efficacy at least six weeks (and probably longer) can be carried with the first aid dressings and can be moistened and immediately bound on the wound by the doctor or the injured person himself.

Still another application of these tampons is possible: When for one reason or another a repetition of the serum becomes desirable, if the wound be still unhealed they can be used for this repetition and thus all fear of dangerous anaphylaxis can be avoided. The absorption is slower, but the effects are also for that reason of slightly longer duration. The lack of danger, the absence of wastefulness, the certain, even if slower, action, and, above all, the ease of application even by the laity are points which favor a thorough trial of these antitoxin tampons.

In conference with the Höchst Farbwerke<sup>5</sup> over this method, they stated that their antitoxin was combined with a certain percentage of glycerin which might interfere with both its drying and preservation. They indicated, further, that a special preparation could be made to meet a demand for such a product.

Further, I have experimentally tested other possible routes of absorption, *e. g.*, through the peritoneal and the pleural cavities, and have not found any advantage over the subcutaneous injections. An attempt was made to confer immunity on guinea-pigs

<sup>5</sup> At this point I wish to express my sincere gratitude to the Höchst Farbwerke, who supplied both the antitoxin and the tetanus toxin used in these series of experiments.

by placing tetanus antitoxin-soaked tampons in the nostrils, but these experiments were entirely unsuccessful.

Returning to the list of failures, as a fifth possible cause may be suggested active surgical interference in the wound. It is an experience which has been repeated several times in cases which have remained for days, weeks, and even months free from any symptoms of tetanus that a severe and even fatal attack of the disease may occur suddenly after some surgical interference, such as amputation, vigorous cleansing, opening abscess pockets, etc. Many of the cases are examples of delayed tetanus. It is difficult to know exactly what occurs under such circumstances. I can only suggest the possibility that such surgical measures either break up surrounding protecting zones of granulation tissue and promote a fresh absorption of tetanus toxin or provide new and better conditions for the development of the tetanus spores lying dormant in the wound. If surgical interference is necessary the antitoxic serum in some form should be repeated before the operation. In cases of this kind, as previously suggested, the dried antitoxin tampons could be used to advantage.

As a sixth possible ground for failure may be mentioned the character of the antitoxin used. It is rather remarkable that of the 66 failures in Table II, 35, or more than one-half, were treated with French antitoxin. Of this number 24 died, which is two-thirds of the total number of deaths (36) tabulated. Here it is of interest to note the report made by Anderson of the United States Public Health Bureau in 1910. He tested the various tetanus antitoxins which were then on the market, and his results showed that while the United States serums varied from 77 units (United States standard) per 1 c.c. for one sample to 769 units for another and the Höchst serum contained 333 units; on the other hand, two samples from the Pasteur Institute and one from another French institute all contained less than 50 units in each cubic centimeter.

Turning now to the tabulated list of failures a more critical analysis can be made. In 6 of the cases (24, 42, 43, 44, 50, 51) the use of powdered antitoxin may well be the cause of non-success. In 10 more (4, 9, 10, 15, 17, 19, 26, 45, 53, 60) one finds excellent examples of delayed tetanus, 8 others (6, 11, 18, 22, 32, 54, 57, 58) show abnormally prolonged incubation periods. Essential details fail in 7 cases (7, 31, 46, 52, 59, 61, 66) and in 4 more (47, 48, 56, 63) the diagnosis is gravely open to question. Of those that remain, if one should judge arbitrarily that after twenty-four hours the antitoxin was probably administered too late, one can exclude 12 further cases (1, 2, 8, 12, 16, 23, 29, 30, 39, 41, 62, 65). Of the 19 cases which remain 1 (3) was treated with Tizzoni's antitoxin, 4 (14, 31, 40, 55) received Swiss serum, 2 (20, 21) German, 2 (27, 28) American, the remaining 10 (5, 13, 25, 33, 35, 36, 37, 38, 49, 64) were all inoculated with French antitoxin. Of the 19 cases 10 died, a mortality of 52 per cent.

Further analysis of these 19 cases does not offer much added value. It is not my aim to "explain away" all cases of failure in the prophylactic treatment of tetanus, for, as has been intimated, it is clear that in the inherent character of the method itself lies always the possibility that failure may enter at any time. I have simply endeavored to show that when the principles which should govern the use of tetanus antitoxin are closely followed not only is the percentage of cases resulting in spite of prophylaxis a very small one, but also as we become more skilful in the preparation of these serums and more rational in the treatment of "tetanus suspicious" wounds, even this percentage may be expected to diminish.

**TETANUS PROPHYLAXIS IN THE PRESENT WAR.** As would be expected the experiences with tetanus in this war are almost as variable and opinions as contrary as have been already noted in private clinical practice. When at the end of the war a complete summary can be made of all the facts concerning tetanus we may look for much valuable data over both preventive and therapeutic treatments. At present most of the statistical evidence is of a much too fragmentary nature to furnish a basis for final judgment.

The first account of tetanus from the prophylactic side was given by Hufnagle in the conference of army surgeons in Namur, November, 1914, at which time he reported that among 2193 wounded treated in the "Festungslazarett" of Namur from September 11 to November 30 there developed 27 cases of tetanus. Beginning the middle of October, all wounded soldiers received a prophylactic injection of twenty units of tetanus antitoxin, and since that time no further cases of tetanus had appeared, although among the 1195 wounded who were treated in the hospital since that date were many who had received very serious wounds.

The results of a collective investigation made by Madelung are of particular interest, especially in relation to prophylaxis. In thirty-seven hospitals where no prophylactic injections were given among 8145 wounded, 63 cases of tetanus developed, a percentage of 7.7. In one hospital where prophylaxis was administered in selected cases from 19,432 wounded occurred 107 cases, or 5.5 per cent. In three other hospitals where protective injections were the routine treatment, among 2104 wounded only 12, or 0.57 per cent. developed tetanus, a striking illustration of the efficacy of antitetanic serum in preventing tetanus when used systematically. From the total number treated only 20 developed tetanus in spite of preventive injections, which in no case were made on the same day that the wound was received, and in half of the cases injections were not given until six days had elapsed.

Walter observed in a hospital in Paris among 270 wounded German prisoners 19 cases of tetanus, and he emphasized the coincidence that all of these wounds were received in the same region near the

Marne. Prophylaxis in those having severe wounds was attempted in the ambulance of the second help line, or at the latest in the hospital, and at the time of his report had given very good success.

Goldscheider declared himself in favor of protective inoculations and gave the results of prophylactic treatment on his service from the beginning of the war until October 1. Among 500 wounded who had been given a prophylactic injection of twenty units of antitoxin, 4, all of whom had shown prodromal symptoms before the injection, alone developed tetanus, but no further cases were seen.

All dirty wounds were treated by Gasch with protective serum, and among 700 of such no tetanus appeared. One soldier, slightly wounded on the toe, who was not injected, developed a fatal case of tetanus.

Sieur, before the French Académie de Médecine in the early part of 1915, stated that although in 1907 certain physicians had not hesitated to doubt the efficacy of prophylaxis, attributing the constant decrease in tetanus to the use of antiseptics on the wounds, he himself credits the absence of it among soldiers of his ambulance corps to the use of prophylactic doses of serum, systematically given and renewed at regular intervals. Among 17,507 wounded only 7 cases of tetanus occurred, in which the first symptoms appeared between twenty-four and sixty hours after. In not one of these cases had prophylactic antitoxin been given.

Behring in a review of the subject emphasized again many of the facts to which he had frequently before drawn attention. Quoting from Dreyfus, he stated that in the Spanish-American war tetanus was completely abolished after the protective injections had been instituted.

One might continue to add further opinions for and against prophylactic treatment of those wounded in war, but the above illustrates sufficiently the views held at this time. It must always be kept in mind that injuries caused by shrapnel, bursting shells, and deeply penetrating bullets are, from the stand-point of tetanus, the most dangerous of all wounds. They are usually deep, contain fragments of clothing, pieces of bone, dirt, or other foreign bodies, and because of their situation demand an expectant rather than a radical treatment. The immediate care of these wounds under the circumstances is not always possible, and shock, loss of blood, and exhaustion all play a part in lowering resistance and causing a condition particularly susceptible to dangerous infections. Antitoxin may be delayed in administration and slow in absorption, while, on the other hand, in a few hours the tetanus spores buried deep in the tissues in the presence of blood clot and other débris have abundant opportunity to multiply rapidly and in many cases toxin production is undoubtedly well advanced at the end of twenty-four hours.

ANAPHYLAXIS. One further point deserves consideration in the discussion of tetanus prophylaxis, and that is the so-called anaphylactic reactions. Following the use of diphtheria antitoxin as a therapeutic agent, innumerable instances of urticarial eruptions, occasional serious attacks of acute intoxication, and rarely even cases of sudden death were reported. The same has been true, although to a far less extent, after the use of tetanus antitoxin. Lapiere collected the cases of what he was pleased to denote "accidents dus á la serotherapie antitetanique." In this collection appear all manner of complications which, because they were preceded by an injection of tetanus antitoxin, were judged by the *post hoc, propter hoc* standard and grouped together as results of the injections. The fact that in the administration of any foreign serum there is a certain possibility of more or less serious intoxication should cause one to exercise the utmost care in attributing to these injections only the consequences which rightly belong to them.

I have previously indicated what occurs when this foreign serum is introduced into the body. Destructive and excretory processes begin at once and continue as long as the serum, as such, remains in the body. But the absorption and excretion are uncommonly slow, owing to the peculiar nature of the substance, and consequently the process of destruction plays an important role. Exactly what this is has not yet been fully explained, but many facts point to the hypothesis that a ferment-like activity operates to split the proteid of the serum into less complex and more readily disposable compounds. Some of these compounds are undoubtedly poisonous for the body. When a guinea-pig receives an injection of horse serum or any alien soluble proteid and, after an interval of ten to twelve days, a second injection of the same substance, violent and even fatal symptoms of intoxication are liable to ensue. This is, of course, the well-known phenomenon of anaphylaxis, and under certain circumstances can occur in human beings following the injection of antitoxin, which is generally a modified horse serum. Probably 50 per cent. of the cases in which this serum is injected show some slight manifestations of this phenomenon.

Most frequently this consists of an erythematous or even a papular urticarial-like itching eruption which develops from forty-eight hours to seven days after the injection, and lasts about thirty-six hours. It may be accompanied by slight fever, headache, malaise, and vague pains in the back and joints. All varying intervening stages may be seen, and the almost invariable rule is rapid and complete recovery. Very occasionally the symptoms are more threatening and simulate those of an acute exanthematous disease with, however, a much shorter course and generally with no disastrous consequences. Still more rarely may be seen the exceptional case in which sudden and overwhelming intoxication occurs, and death

may take place a few minutes after the injection. Such a case in which death occurred within five minutes after a prophylactic injection of tetanus antitoxin was the subject of a medicolegal investigation in the state of Minnesota. Another similar case is reported by Riche in 1912: A girl, aged eight years, after an injury of the hand, was given 10 c.c. of antitetanic serum. A few hours later symptoms of collapse ensued and she died without in any way responding to stimulants.

That such occasional accidents should have no bearing on the use of diphtheria or tetanus antitoxin hardly needs to be argued. The fact that in the use of antitetanic serum serious consequences are extremely rare and with the purification of the antitoxin are becoming increasingly rarer is a hopeful sign that even this disadvantage may finally be entirely overcome. By carelessly ascribing to antitoxin injections all sorts of unreasonable and often absurd consequences, much harm may be done not only among the laity, but also among the medical profession. For example, in Lapierre's collection is a case reported by Camus where death, undoubtedly caused by osteomyelitis and sepsis, was credited to antitoxin which had been injected three days before!

CONCLUSIONS. 1. The most ideal and perfect protection against tetanus is the protection of active immunity produced before the infection has occurred. This admittedly is not yet practical, but deserves further consideration and research.

2. In the large majority of cases the subcutaneous injection of twenty units immediately after the injury will prevent with certainty the occurrence of tetanus. The delay of a few hours in making the injection may mean the loss of life.

3. Local applications of fluid antitoxin on the wound are efficacious but unnecessarily wasteful and not always practical.

4. In cases where injections cannot readily be made, especially in time of war, the immediate application to the wound of dried antitoxin tampons moistened by clean fluid may be used as a temporary substitute until fluid antitoxin can be injected.

5. Powdered antitoxin on the wound is not, as a rule, dependable. Its one useful field is perhaps the prevention of tetanus neonatorum.

6. Certain failures are to be expected in the prophylactic treatment of tetanus as carried out at the present time. Occasional cases of tetanus will develop in spite of the most careful precautions.

7. The protection afforded by antitoxin lasts from two to three weeks. Hence in cases of protracted suppuration or where for other reasons secondary surgical interference is contemplated either second injections of antitoxin should be made or dried antitoxin tampons freshly moistened should be placed on the wound.

8. Certain complications, most frequently urticarial-like eruptions, and very rarely more serious results may follow injections of antitoxin.



Finally, I wish to emphasize once more that we are not dealing with an ideal remedy. There are few if any such known to man. Hence one must frankly face and admit its disadvantages. At the same time neither hasty clinical opinions based on empiricism nor narrow-visioned laboratory theories can alone guide one's judgment. A calm recognition of all the facts, the disadvantages and the advantages, and the reasons for both will surely lead to an eventual proper line of action based, as it always should be, on the broad foundation of reason and experience.

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## STUDIES ON THE LOCALIZATION OF CEREBELLAR TUMORS: II. THE POINTING REACTION AND THE CALORIC TEST.

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THE purpose of this paper is to discuss the importance of the pointing reaction (Barany) and the caloric test in the diagnosis of new growths in the posterior fossa. It is based upon an analysis of the records of 31 cases of cerebellar or extracerebellar tumor.

The patients were in the neurological services of Dr. Cushing at the Johns Hopkins Hospital and at the Peter Bent Brigham Hospital. With a few exceptions they have all been personally studied by the writer. In 5 cases the examinations were made by Dr. Cushing and Dr. S. J. Crowe at the former institution.

The diagnosis and localization of the lesions were confirmed in all of the cases either at operation or on postmortem examination. All records have been excluded which showed that the disease had extended into other parts or which included additional factors likely to confuse the symptom-complex.

The present report is one of a series of studies which were suggested by the difficulties attending the localization of many cerebellar tumors.<sup>1</sup> Notwithstanding the important contributions which have appeared since Barany suggested the use of the caloric and the pointing tests, there is still much difference of opinion in regard to the interpretation of these and other cerebellar signs. For purposes of analysis, new growths in the posterior fossa have been divided into five groups: tumors of the vermis, tumors occupying one hemisphere, tumors involving most of the cerebellum, cerebellopontine tumors, and extracerebellar tumors lying inferior to the vermis.

The cases are numbered and presented in the same order in the reports of the pointing reactions and the caloric tests. In this way the data from each patient in the two groups may be compared.

The pointing reactions and the caloric tests were carried out in the manner described by Barany.<sup>2</sup>

<sup>1</sup> Grey, Studies on the Localization of Cerebellar Tumors: I, Staggering Gait, Limb Ataxia, the Romberg Test, and Adiadochocinesia, *Jour. Nerv. and Ment. Dis.*, 1915, xlii, 670. II, On Localization of Function in the Canine Cerebellum, *ibid.*, to appear soon. Studies on the Localization of Cerebellar Tumors: III, Posterior New Growths without Nystagmus, *Jour. Am. Med. Assn.*, 1915, lxx, 1311.

<sup>2</sup> *Wien. klin. Wchnschr.*, 1912, xxv, 2033 and *Tr. Internat. Cong. Med.*, 1913, Lond., 1914, Sect. xi, *Neuropath.* pt. 2, 53; Friesner and Braun, The Functional Tests of the Static Labyrinth in Neurological Diagnosis, *New York Med. Jour.*, 1914, c, 369; Layton, Examination of the Internal Ear and Hind Brain by Stimulation of the Vestibular Nerve, *Clin. Jour.*, London, 1914, xliii, 193.

NEW GROWTHS INVOLVING THE VERMIS. *Pointing Reaction.* The pointing reaction was tried with three patients having median tumors involving the vermis. In each case the examination was made previous to operative measures. (1) One (solitary tubercle measuring 3 cm. across) pointed correctly in all of the tests during three separate investigations.

(2) A second (cyst lying more to the left of the midline—about 30 c.c. fluid) likewise performed each of the reactions correctly on two different occasions, but thirteen days following a suboccipital decompression with emptying of the cyst both arms were found to deviate outward. The head also showed a slight pointing error—to the patient's right.

(3) In the third patient (large glioma involving all of the vermis and the dentate nucleus of each hemisphere) the right leg occasionally deviated inward. The right arm also showed a pointing error upward.

*Caloric Test.* The three patients mentioned above were investigated with the caloric test. In the first of these (1), three separate examinations were made on different days. No spontaneous nystagmus was ever elicited. During all three examinations, stimulation of the left labyrinth provoked a more marked nystagmus than stimulation of the right. In the two earlier tests, irrigation of the right ear resulted in reaction movements in the right arm only, whereas irrigation of the left caused the appearance of typical reaction movements in both upper limbs. In the third examination the same type of reaction followed the irrigation of each ear.

(2) The second patient was studied on two separate occasions previous to his operation and once following it. A moderate spontaneous nystagmus was present at times with its quick component directed to the left. Looking to the left brought out slower and coarser jerks than looking to the right. Practically the same type of reaction resulted from the stimulation of the two labyrinths. This consisted of a rather marked nystagmus and normal reaction movements. The artificial nystagmus did not completely obliterate the spontaneous jerks. In the third examination, conducted on the thirteenth day after operation, the nystagmus resulting from the irrigation of the left ear was much less marked than that which appeared from the opposite side. On stimulating the left labyrinth, however, reaction movements were obtained in all of the parts, whereas on stimulating the right side the reactions appeared only in the homolateral limbs.

(3) The third patient was examined only once, as he died of respiratory failure some hours after admission. During the investigation there was nothing to suggest an agonal condition, as he sat in a chair without apparent discomfort, and was able even to walk across the room on his hands and knees.

When the patient looked forward a slight nystagmus was visible,

the quick component being directed to his left. Coarse jerks of equal range and rate appeared on looking to either side. On stimulating the labyrinths, well-marked reaction movements appeared in the head, trunk, and limbs of either side. The degree of nystagmus was likewise increased, but the artificial never completely obliterated the spontaneous jerks.

Hearing was not affected in any of these patients. In one no subjective discomforts followed the irrigation of either ear. A slight dizziness, however, resulted from the tests in the other two patients.

**NEW GROWTHS INVOLVING ONE HEMISPHERE.** *Pointing Reaction.* This test was tried on 10 patients. Of these 6 were investigated previous to operative interference. The results from the latter were as follows. (1) One (large glioma) performed the tests correctly with his arms, but the leg opposite to the side of the lesion deviated somewhat outward. Following the operation both arms deviated outward and downward, and the head inclined slightly away from the lesion. (2) The second patient (large gliomatous cyst) showed a pointing error inward with both arms. (3) The third (large gliomatous cyst) was studied on seven separate occasions. In the first examination, made previous to operative interference, there was an outward deviation of the arm homolateral to the lesion. Later, following a subtemporal and a suboccipital decompression, the test was performed correctly during three examinations, made at intervals of a month. Still later both arms deviated slightly outward and upward. In two additional months both were again normal in their movements. The final examination, made after five weeks, showed a slight inward and downward deviation of the arm contralateral to the side of the tumor. (4) (Multiple tubercles involving practically one entire hemisphere). Correct pointing reactions were found during three examinations on separate days. (5) The fifth (large endothelioma occupying but not invading lateral half of hemisphere) showed no pointing errors in any part. (6) In the sixth patient (large gliomatous cyst) during the first examination the reactions were all normal. On the following day, however, the left arm showed a pointing error outward. Tests made two days later again showed normal reactions.

This test was first used subsequent to an exploratory operation in 4 patients. Five months following a suboccipital decompression (7) one of these (large glioma) pointed outward with the arm homolateral to the new growth and inward with the opposite arm. Six months later the homolateral arm still inclined outward. The opposite arm, however, pointed correctly. Twelve months subsequent to a suboccipital decompression (8) a second patient (large glioma) showed an outward pointing error of both arms, more marked on the side opposite to the lesion. During a third admission (just previous to the extirpation of a large glioma) the pointing

test was performed correctly on either side. The third and fourth cases were investigated two years and six years respectively after operations in which gliomatous cysts were evacuated. In the former (9) the arm homolateral to one lesion deviated somewhat outward. In the latter (10) during one examination both arms pointed correctly; in a second, however, there was an inward pointing error on the side of the cyst.

*Caloric Test.* This test was used in all of the 12 patients comprising this group. In 9 of these, examinations were made previous to any operative interference. Practically a normal response followed the irrigation of each ear in 2 of the latter (2) and (11), and gliomatous cyst the size of a hen's egg. The remaining 4 reacted as follows. (1) One showed reaction movements on each side and some nystagmus when the labyrinth contralateral to the lesion was stimulated, but nothing when the homolateral side was irrigated. About four weeks after the extirpation of a large glioma from this patient, reaction movements and nystagmus were elicited through both ears. (3) A second showed reaction movements on either side and an increased nystagmus during the irrigation of the contralateral ear. Neither of these was apparent, however, when the opposite ear was stimulated. Six months subsequent to a subtemporal and a suboccipital operation, practically the same responses were obtained during two separate examinations. (4) In a third, irrigation of the homolateral ear provoked no nystagmus but caused the appearance of reaction movements on both sides—to a less extent in the homolateral arm. Irrigation of the contralateral ear resulted in well-marked nystagmus and good reaction movements in all the parts. (5) A fourth responded with nystagmus and reaction movements from the stimulation of both labyrinths. From the homolateral labyrinth, however, both were much less marked. (6) The reactions in the fifth patient were very interesting. Stimulation of the homolateral labyrinth resulted in slight reaction movements in the arm on that side. None appeared on the opposite side. The irrigation, furthermore, had no effect on the spontaneous nystagmus. Stimulation of the contralateral labyrinth caused marked reaction movements in the arm of that side, but none in the opposite limb. A coarse nystagmus also appeared. A second examination made on the following day afforded the same results, except that no reaction movements appeared in either arm subsequent to the irrigation of the homolateral ear. During both examinations the homolateral ear was found to be deaf. Preceding the onset of this illness the patient apparently heard equally well with both ears.

(8) A sixth showed less nystagmus and vaguer reaction movements when the labyrinth on the side of the lesion was stimulated. During a second admission subsequent to a suboccipital decompression irrigation of each ear provoked slight and moderate nys-



tagmus. The latter was more marked when the contralateral labyrinth was stimulated.

(12) A seventh (large gliomatous cyst) gave no response from the irrigation of either side.

(7) (9) (10) In 3 patients this test was first used five months, two years, and six years respectively following suboccipital operations. Stimulation of the homolateral labyrinth in the first of these (7) caused slight nystagmus and no reaction movements in either arm, but on the opposite side it resulted in more marked nystagmus and good reaction movements in both arms. Six months later during two examinations (on different days) practically the same results were obtained. Within a week of these investigations a huge glioma was removed from the right hemisphere.

Irrigation of each ear in the second (9) resulted in some nystagmus. There were reaction movements on both sides when the contralateral labyrinth was stimulated, but none appeared in either arm when the homolateral was stimulated. (10) The third patient was irrigated both with cold and with combined hot and cold solutions. While they increased the spontaneous nystagmus from each ear no reactions were noted in any limb, in the head, or in the trunk. A repetition of this examination made one year later gave the same results.

As a rule, no subjective discomforts resulted from the irrigations; occasionally some dizziness followed the stimulation of the ear contralateral to the lesion. Nausea and vomiting appeared in none of these cases. In 3 patients (1) (6) (12) hearing was impaired on the side of the disease. The external and middle ears in all of the cases appeared normal.

NEW GROWTHS INVOLVING NEARLY THE ENTIRE CEREBELLUM.  
*Pointing Reaction.* The pointing test was used with 5 patients who subsequently were shown to have had tumors occupying most of the cerebellum at the time of the investigations. All of the reactions were normal in the first of these (1). Several weeks after a suboccipital operation, however, in which the greater portion of an extensive glioma was removed (involved the vermis, all of the left and most of the right hemispheres), the left arm deviated definitely outward. (2) In the second patient (multiple tubercles of the vermis and left hemisphere) the tests were correctly performed in the limbs, head, and trunk. Two repetitions of the examination made at intervals of five to six weeks gave the same results. (3) In the third subject (bilateral gliomatous cysts) the first investigation elicited no abnormal reactions, but a month later there was an outward pointing error of the left arm and an outward and upward error of the right. A year following these studies, just previous to a second operation, all of the reactions were found to be normal during two separate examinations. The 2 remaining patients were first studied some time subsequent

to suboccipital operations. (4) One of these had been treated surgically on two occasions, the first a suboccipital decompression three years previously, and the second a partial extirpation of a huge glioma involving the whole vermis, left hemisphere and part of the right one year previously. The pointing tests were all well done during several examinations. At autopsy a few weeks later the growth was found to be very extensive—merely a thin shell of cortex remained. (5) In the second of these 2 patients a large infiltrating glioma had been removed from the cerebellum four years previously. When tested the right arm was found to deviate inward. The left reacted well in spite of the fact that it was much more ataxic than the right. This same inward error of the right upper extremity was manifest during subsequent examinations.

*Caloric Test.* (1) The first patient showed a spontaneous nystagmus on looking to either side, coarser to the left. On irrigating the ears in turn an outspoken nystagmus appeared—more marked from the left. As was frequently the case, the spontaneous jerks were not entirely obscured when the patient looked toward the labyrinth which was being stimulated. The caloric test on the right side resulted in reactions in the right arm only. On the left it elicited no reaction movements. The same spontaneous, outward deviation of the latter, however, persisted (see (1) under pointing tests). Some weeks subsequent to a partial extirpation of the tumor, stimulation of the labyrinths provoked a nystagmus, more marked, as in the original examination, when the left side was irrigated. No reaction movements were now apparent on testing the right ear, but on irrigating the left the right arm responded. The left arm continued to show the same pointing error outward. (2) The second subject gave practically normal reactions. There were good reaction movements in all of the limbs, in the head, and in the trunk. (3) In the third patient there was a definite difference in the reactions from the two sides. Irrigation of the right ear resulted in outspoken nystagmus, considerable dizziness, and well-marked reaction movements. Irrigation of the left, on the contrary, provoked only a slight nystagmus, no dizziness and no reaction movements. Occasionally a spontaneous nystagmus appeared with its quick component directed to the right. More marked jerks were evident when the eyes were turned to either side—coarser to the right. A month later, on repeating the tests, moderate reaction movements were obtained through the left labyrinth, and the patient experienced some dizziness. Both, however, were less marked than those arising from the opposite side (right labyrinth). A third examination made in the following year, just previous to a second operation, brought out reaction movements from the right labyrinth but none from the left. (4) (5) In the remaining 2 patients of this group, both of whom had been operated upon several years previously, no response was obtained from the stimulation of either labyrinth.

CEREBELLOPONTINE NEW GROWTHS. *Pointing Reaction.* This test was used in 8 patients having cerebellopontine new growths. (1) In the first the preliminary examination elicited normal pointing reactions. On repeating the tests several days later there was an outward pointing error in the arm homolateral to the tumor. (2) The second patient was studied on four different occasions—all within four months—the first being previous to operation and the others between the first and second attempts at tumor extirpation. In all four examinations, notwithstanding a marked ataxia in the limbs homolateral to the lesion, the tests were performed correctly. The third, fourth, fifth, seventh, and eighth patients were only tested before operation. In 2 of these (3) (5) the pointing reactions were well done, though a marked unilateral ataxia existed at the time. In another (4) there was an inward and downward pointing error of the arm contralateral to the tumor. Another (7) (cerebellopontine cyst) showed a downward pointing error of the homolateral arm. The following day all of the reactions were normal. The third examination, made twenty-four hours later, revealed an inward pointing error of the homolateral arm. The last of this group (8) gave normal reactions.

(6) The sixth patient showed an outward pointing error of the arm contralateral to the growth during the preliminary tests. Two days later the pointing reactions were well done on either side. The same normal responses followed in a third examination made one month subsequent to the extirpation of the new growth. But in six additional weeks the arm homolateral to the diseased side showed an inward and upward error.

*Caloric Test.* Nine patients with cerebellopontine tumors were investigated with the caloric test. (1) The first showed no response of any kind when the ear homolateral to the lesion was irrigated. Irrigation of the opposite meatus, however, resulted in moderate nystagmus and fairly marked reaction movements. There was great impairment of hearing on the tumor side. (2) The second patient reacted normally when the labyrinth contralateral to the tumor was stimulated; but no reaction movements, no subjective discomfort, and only slight nystagmus resulted when the opposite side was irrigated. A spontaneous nystagmus with its quick component directed toward the ear opposite the lesion was not entirely obliterated by the artificial jerks, *i. e.*, when the patient looked toward the ear which was being irrigated. After a suboccipital decompression, reaction movements appeared in the arm homolateral to the tumor when the test was tried in the ear of the same side. A more marked nystagmus also followed this irrigation. In eight additional weeks just previous to a second exploratory operation the responses from the two labyrinths were alike. There was a rather marked nystagmus, but neither reaction movements nor subjective discomforts. Hearing in the homo-

lateral ear was greatly impaired. The caloric tests in the third patient (3) were without visible effect. Neither nystagmus nor reaction movements resulted from the stimulation of either labyrinth. (4) The fourth subject gave no response during the irrigation of the homolateral ear, but when the opposite side was irrigated, nystagmus and definite reaction movements (in both arms) appeared. The patient listed as fifth (5) in the report of the pointing tests was not investigated with the caloric reaction. The sixth patient (6) examined just previous to the extirpation of a lateral recess endodermioma which lay deeply imbedded in the hemisphere showed no spontaneous nystagmus. From the labyrinth opposite the lesion there followed a normal response—nystagmus, general reaction movements, considerable dizziness with some slight nausea, and falling dependent upon the position of the head. From the tumor side no response whatsoever was elicited. Hearing was only slightly affected in this ear. Irrigation of the labyrinths of the seventh patient (7) resulted in nystagmus and bilateral reaction movements from both sides. The homolateral ear, however, was deaf. A second investigation made two days later afforded the same results except that the nystagmus was considerably longer in appearing when the homolateral ear was irrigated; but the reaction movements, on the contrary, resulting from this stimulation, were more marked than those which followed the stimulation of the contralateral labyrinth. A single examination of the eighth patient (8) showed good reaction movements and coarse nystagmus when the contralateral ear was irrigated, but no nystagmus and slight reaction movements when the homolateral side was irrigated. The homolateral ear was deaf (deafness appeared during this illness). Dissimilar reactions were obtained from the two labyrinths in the 2 remaining patients (9) (10). While irrigation of the contralateral ear affected the spontaneous nystagmus and caused some dizziness, irrigation of the homolateral side had no apparent effect. The reaction movements were not investigated. Hearing was seriously impaired on the tumor side in both cases.

**EXTRACEREBELLAR NEW GROWTHS LYING INFERIOR TO THE VERMIS.** *Pointing Reaction.* The pointing test was studied in 1 (1) of the 3 patients belonging to this group. During the first and second examinations (several days apart) normal reactions were obtained from the limbs, the head, and the trunk. During the third examination, however, both arms deviated outward. Subsequent to a combined exploratory and decompressive operation (large glioma) the tests were again performed correctly.

*Caloric Test.* A limited spontaneous nystagmus was noted in the patient (1) mentioned above. It was only visible when the eyes were turned toward his right. During the first examination there appeared with each irrigation slight reaction movements in the two arms, a very moderate nystagmus, and a tendency to fall

in a direction dependent upon the position of the head. The patient experienced some dizziness. The second examination (two days later) yielded somewhat different results. No reaction movements in either arm were visible and there was no inclination to sway or fall. In 2 other patients (2) (3) the vestibular responses were approximately normal.

**DISCUSSION.** While pointing errors of the arms appear in many affections of the central nervous system,<sup>3</sup> Barany believes that they always arise through changes either in the cerebellar cortex or in the efferent fibers passing from it. He explains the occurrence of pointing errors in patients with lesions elsewhere in the brain by assuming that such errors result from the cerebellum indirectly through pressure (*Fernwirkung*).<sup>4</sup> If a pointing error is present but the normal reaction movements in the affected arm are still procurable, it indicates that the error is due to pressure exerted upon the cerebellum from a distance. When the reaction movements are all elicited except the one opposite to the pointing error it indicates, on the other hand, that the deviation is the result of a cortical lesion in the cerebellum.

It has been shown that after a time the spontaneous errors disappear. To demonstrate the defect in such a case it is necessary to make use of the caloric tests. In cerebellar disease Ruttin, Neumann, Oppenheim,<sup>5</sup> and others describe an excessive excitability of the vestibular apparatus on the affected side (nystagmus and reaction movements).

In most of the patients reported here with cerebellopontine tumors the responses from the two labyrinths were sufficiently different to be of supplementary use in localizing the disease. In a few patients with new growths in one or the other hemisphere the reactions were likewise helpful. Pointing errors elicited in the arm homolateral to the lesion were shown to have a localizing significance by the absence of local reaction movements in a direction opposite to the spontaneous deviation. The decreased response from the labyrinth on the diseased side was also helpful in a few instances in suggesting the side of the new growth. In the majority of the cases, however, the results were ambiguous and afforded no assistance in establishing a diagnosis. In fact, in numerous instances the conclusions drawn from these results were at variance with the other physical findings, and had any great reliance been placed in them, would have led to erroneous results.

From such experiences it is evident that these tests are likely to give less consistent results in patients with tumor than in

<sup>3</sup> Rothmann, The Differential Diagnostic Significance of the Barany Pointing Reaction, *Neurol. Centralbl.*, 1911, xxxiii, 3.

<sup>4</sup> Barany, Additional Researches on the Relations between the Vestibular Apparatus and the Central Nervous System, *Wien. med. Wchnschr.*, 1912, lxii, 3210.

<sup>5</sup> *Lehrbuch der Nervenkrankheiten*, 1913, p. 920.

patients with other types of lesion. Barany<sup>6</sup> regards fluctuations in pointing errors and in reaction movements as a sign that such deviations from the normal are due to the cerebellum only indirectly—through pressure exerted upon it from a distance. In the patients with verified cerebellar new growths reported here there were numerous instances in which the reactions varied from one examination to another.

The explanation of these variations probably chiefly concerns two factors. Tumors in the posterior fossa rapidly lead to a condition of secondary internal hydrocephalus. This means a general increased intracranial tension. Symptoms and signs which might arise from circumscribed cerebellar lesions, in the presence of such an increased pressure, probably undergo considerable alteration and become untrustworthy for diagnostic purposes. In the second place most of the tumors which directly affect the cerebellum are grossly mutilating in their growth. Great areas are often involved and anatomical landmarks are effaced. From such an involvement of centres—often rapidly increasing as the tumors spread—we might expect confusing results when functional tests are tried.

The degree of intracranial tension was estimated in each case. For this purpose both the pressure at operation and the swelling of the optic nerve heads were used. It seemed possible that some relationship might exist between the degree of intracranial tension and the nature of the responses. No satisfactory evidence of such a relationship, however, was found.

As Barany,<sup>7</sup> Friesner and Braun,<sup>8</sup> and others have pointed out, in the reaction movements we have a means of differentiating between the balance disturbances due to labyrinthine disease and those of another origin. When the labyrinth is injured, Wilson and Pike<sup>9</sup> and others have shown that the tendency to fall is always in the direction of the slow component of the nystagmus. When the cerebellum is involved, on the other hand, the falling is independent of the direction of the spontaneous nystagmus. The direction of the falling, furthermore, does not change with changes in the position of the head. Barany found that patients with cerebellar disease fell mostly toward the involved side.

In the cases reported above, the direction of falling was almost invariably independent of the direction of the nystagmus and the position of the head. It likewise appeared to bear no relation to the side of the lesion. The latter feature has been discussed more fully in another place.<sup>10</sup> Frequently irrigation of the homolateral

<sup>6</sup> Demonstration of Patients, with Comments, *Wien. klin. Wchnschr.*, 1911, xxiv, 1173.

<sup>7</sup> The Vestibular Apparatus and the Cerebellum, *Brit. Med. Jour.*, 1910, ii, 1215.

<sup>8</sup> *Loc. cit.*

<sup>9</sup> Vertigo, *Jour. Am. Med. Assn.*, 1915, lxiv, 561.

<sup>10</sup> Grey, *loc. cit.*

ear had no effect on the spontaneous falling, whereas stimulation of the opposite labyrinth resulted in a labyrinthine type of falling.

Neumann,<sup>11</sup> among others, believes that each cerebellar hemisphere exercises control of an inhibitory nature over the nystagmus directed toward its own side. Tumors and other lesions which destroy a hemisphere abolish this inhibitory influence. Accordingly, in such cases, when the labyrinth contralateral to the disease is stimulated with cold water a nystagmus toward the affected side follows which outlasts a normal reaction by several minutes. This so-called enduring nystagmus may last from five to fifteen minutes or more. In the cases with hemisphere tumors encountered here no considerable endurance of the nystagmus was noted. Frequently differences were observed in the responses from the two ears, but usually these were due to a diminished reaction on the diseased side. These findings seem to be in accord with the results obtained by Bauer and Leidler<sup>12</sup> from extirpating different parts of the cerebellum in animals. They found that so far as the cerebellum itself is concerned an increased excitability of the vestibular apparatus only appeared from lesions of the vermis.

Barany<sup>13</sup> and others have found that most of the cases with brain tumor in which there was a considerably increased pressure in the posterior fossa experienced very little subjective discomfort from the caloric tests. The appearance of much dizziness and nausea and of vomiting speaks against a process in the posterior fossa. The results from the irrigations reported here entirely agree with these experiences.

**CONCLUSIONS.** The caloric test has proved to be an important means of differentiating labyrinthine from intracranial disease. Together with the pointing reaction, this test has been found of value, furthermore, in localizing circumscribed lesions in the cerebellum. The present report has to do with the results obtained from using these tests in 31 patients with cerebellar or extracerebellar tumor.

In most of the patients having cerebellopontine new growths and in certain of those with tumors of one or the other hemisphere, the reactions were sufficiently characteristic to be of supplementary value in localizing the disease. This suggests the desirability of a further study of these tests in neurological diagnosis. In other patients with intra- or extracerebellar tumor, on the contrary, the results were often ambiguous and afforded no assistance in establishing a diagnosis.<sup>14</sup> In fact, in numerous instances the con-

<sup>11</sup> Quoted by Friesner and Braun, *loc. cit.*

<sup>12</sup> Concerning the Effect of Excision of Different Portions of the Brain on the Vestibular Eye Reflex, *Arch. a. d. Neurol. Instit. a. d. Wiener Univ.*, 1912, xix, 155.

<sup>13</sup> *Loc. cit.*

<sup>14</sup> Since this paper was prepared for publication the pointing reaction and the caloric test have been studied in about a dozen and a half additional certified cases of cerebellar tumor. The conclusions drawn from these examinations differ in no essentials from those outlined above.

clusions drawn from these results were at variance with the other physical findings, and, had any great reliance been placed in them, would have led to erroneous results.

There are probably a number of factors responsible for the occurrence of atypical reactions in patients with certified cerebellar tumors. As the more important we may mention first, the great increase in intracranial pressure due to an internal hydrocephalus which ultimately accompanies new growths in the posterior fossa, and second, the diffuse nature of many of the tumors common to the cerebellum.

## A CASE OF PRIMARY SPLENIC HODGKIN'S DISEASE.

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SINCE 1832, when Hodgkin reported 7 cases of the condition which now bears his name, the etiology has been unknown, and until recently its pathology was ambiguous. But through the efforts of Reed, Longcope, Andrews and others an histological picture has been established which undoubtedly places it among the disease entities and separates it from several conditions with which it has been confused. Most prominent among these are tuberculosis, lymphosarcoma, and pseudoleukemia.

Sternburg,<sup>1</sup> in 1899, held that it was a special glandular form of tuberculosis, just as lupus was a special cutaneous manifestation. This view is no longer tenable in light of the proof that lymphatic tuberculosis and Hodgkin's disease may coexist. At the time this case was autopsied the diphtheroid organism had not been promulgated as the probable cause of the condition. The etiology is far from settled yet. The later results of the vaccine treatment have not given the ground for hope that some of the earlier over-enthusiastic reports afforded.

Characteristically, the disease has its origin in the cervical lymph glands, but cases of anomalous origin have been reported from time to time. Parkes Weber<sup>2</sup> reports a case primary in the bronchial glands. The first signs in this case were cyanosis and edema of the extremities, with osteo-arthropathy as a prominent terminal feature. Symmers<sup>3</sup> reports 2 cases primary in the retro-peritoneal lymph nodes, and others having this origin have been reported previously.

<sup>1</sup> *Ztschr. f. Heilk.*, 1898, xlx, 21.

<sup>2</sup> *Proc. Royal Soc. Med.*, 1909, ii, Clin. Sec., 66.

<sup>3</sup> *Arch. Int. Med.*, 1909, iv, 218.



Lyon<sup>4</sup> states that there is no evidence that a primary splenic form of Hodgkin's disease exists. Reed<sup>5</sup> says that we know of no cases where the pathological anatomy was described in sufficient detail to permit of a positive diagnosis in which the disease commenced elsewhere. Longcope<sup>6</sup> describes a case originating in the retroperitoneal lymph nodes. Simmons<sup>7</sup> also reports 2 cases primary in the retroperitoneal lymph nodes.

But after a thorough search of the literature I am unable to find any case of this disease that can unequivocally be demonstrated to be of primary splenic origin. There are only two which make such a claim, both of which I shall subsequently discuss in connection with the analysis of the findings of this case, which I will now describe in detail.

**CASE HISTORY.**—On October 25, 1910, C. L., female, aged seventeen years, entered the University Hospital (Homeopathic). At that time she complained of severe pain in the left hypochondriac region. They were more frequent at the menstrual periods. She had had the diseases of childhood, measles, chicken-pox, etc.

Her present illness dated from February, 1910, when she had chills and fever, with pain in the left side, from which she was in bed for one week. Since then she has had intermittent chills and fever. Her menstruations, which were normal in every respect, began when twelve years of age, but since February, 1910, she has had amenorrhea with vicarious epistaxis. At the time of entering the hospital there was copious epistaxis present every morning, and more rarely through the day.

In September, 1910, she contracted a cold which seemed to settle in the left hypochondrium, causing pain which has been almost constant and accompanied by a persistent cough.

She was first sent to the Gynecological Clinic, when Dr. Kinyon operated for atresia of the vagina, removed cervicovaginal adhesions, and freed an adherent clitoris. Five days after the operation the temperature started to rise, reaching  $103.5^{\circ}$  on the ninth day after operation, and staying at this point for three days. It then gradually receded, reaching normal in nine days. Previous to this operation the urine was negative and the blood examination was as follows: reds, 4,500,000; whites, 3000; hemoglobin, 90 per cent.

Differential count of leukocytes: Large lymphocytes, 3.3 per cent.; small lymphocytes, 11.7 per cent.; mononuclears, 2 per cent.; polymorphonuclears, 80.5 per cent.; eosinophiles, 2 per cent.; basophiles, 0.5 per cent.; myelocytes, none; count of 400 cells, 100 per cent.

On November 8, 1910, the count was: reds, 2,800,000; whites,

<sup>4</sup> Osler's Modern Medicine, p. 675.

<sup>5</sup> Johns Hopkin's Hosp. Rep., 1902, x, 133.

<sup>6</sup> Bulletin Ayer Clinical Laboratory, Pennsylvania Hospital, 1903, vol. i iv.

<sup>7</sup> Jour. Med. Research, 1903, ix, 325.

1000; hemoglobin, 75 per cent. Differential count: small lymphocytes, 11 per cent.; large lymphocytes, 2.5 per cent.; mononuclears, 1.5 per cent.; polymorphonuclears, 84 per cent.; eosinophiles, 1 per cent. myelocytes, none; count of 500 cells, 100 per cent.

On November 15, 1910, the count was: reds, 2,600,000; whites, 800; hemoglobin, 60 per cent. The differential was in substance the same as the above. The urine was still negative, and a von Pirquet test was also negative after ninety-eight hours.

On November 15 she was transferred to the Surgical Clinic, when she came under the care of Dr. Dean T. Smith. A physical examination showed an enlarged spleen and bilateral enlargement of the inguinal lymph nodes. The axillary glands as well as the cervical were negative. There was an area of dulness over the left lung, extending to the third rib in the sternal line, and going slightly higher in the midaxillary line. Over this area the voice sounds and tactile fremitus were absent, but distant bronchial breathing was noticeable.

On November 18, 1910, Dr. Smith performed a splenectomy, the patient reacting nicely. On the second day following the operation the temperature started to rise, and on November 24 had reached 104°. Up until this time the pulse had stayed with the temperature, but at this point they parted, the pulse going up to 150 and the temperature gradually falling to 100° on November 30, at which time the patient died. The blood count showed: reds, 2,900,000; whites, 11,500; hemoglobin, 70 per cent. Differential count was not materially altered from the other counts.

**AUTOPSY PROTOCOL.** *External Examination, General.* Build: Frame small; length, 150 cm. Eyes: Blue, eyeball gray; pupils dilated. Neck: Negative. Abdomen: Oval above the level of the ribs. Anomalies: None on external examination. Surgical wounds: 3 cm. to left of ensiform and one finger-breadth below rib is a surgical wound 19 cm. long. The uppermost 11 cm. has stitches and is not united. The rest of the wound is united superficially except at the lower part, where 8 cm. is open. Scars: Scar on forehead above eyebrows. Skin: Pigmentation slight. Hair: Light in color, small in amount; pubic hair shaved. Teeth: Good. Mucous membranes: Pale; conjunctivæ pale. Muscles: Slight muscular development. Rigor mortis: In jaw. Panniculus: Moderate in amount. Edema: Slight edema above ankles. Body heat: Present. Hypostasis: Purple hypostasis on buttocks and back. Inguinal lymph nodes large and palpable. Cervical and axillary lymph nodes not palpable.

*Thorax and Abdomen (Main Incision).* Panniculus: Moderate amount, 1.5 cm. thick over abdomen. Musculature: Scant in amount, good red color; little blood escapes from incision. Abdominal cavity: Contains about 200 c.c. of clear fluid with fibrin

flakes. Small and large intestines distended by gas. Surface moist and shining. Adhesions about coils of intestines and about the cecum; fibrinous exudate. Appendix and cecal region bound down by easily-broken adhesions. Purulent exudate. Appendix points inward to the pelvis, behind uterus. Cecum adherent to the upper border of broad ligament, lying in a walled-off area in which lies a purulent exudate. Parietal peritoneum loosely adherent to the capsule of the liver on right, and capsule more adherent along the upper end of the surgical wound. Omentum: Spread over intestines down to the lower part of the pelvis and adherent loosely to coils of intestine. Congested; vessels dilated; adherent along wound. Position of abdominal organs: Liver four finger-breadths below ensiform at median line, two finger-breadths below rib border on right nipple line. Transverse colon at level of umbilicus. Stomach four finger-breadths above the ensiform. Position of diaphragm: Dome of diaphragm, fourth rib on right, fifth rib on left. Mammæ: Free from tumor. Gland tissue slight. Right clavicle dislocated at sternoclavicular articulation. Sternum: Negative. Enlarged lymph node at upper end.

*Thorax.* Thoracic cavity: Left plural cavity contains 1 liter straw-colored fluid; lungs do not recede from wall. Left lung loose adhesions, especially over dome of diaphragm and at upper pole. Right lung more adherent at lower margin. No fluid in right pleural cavity. Apex of heart in fifth intercostal space in nipple line. Anterior mediastinum: Fat scant in amount. Thymus: No gross evidence of thymus. Pericardium: Not adherent to epicardium. Fluid not increased, about 5 c.c. clear, straw-colored fluid, no flakes. Heart: On cutting the great vessels there is a large amount of postmortem cruor. Heart size of right fist of the cadaver. Surface shining. No sclerosis. Right heart: Right ventricle contains postmortem clot. Papillary muscles well developed. Left heart: Left ventricle contains a quantity of cruor. Small amount of agonal clot in lower part. Wall, 1.5 cm., 2 to 3 mm. fat. Cardiac orifices and valves: Mitral valve admits two fingers; flaps not thickened; no vegetations. Tricuspid admits two fingers; flaps negative. Pulmonary admits thumb; negative. Aorta admits thumb; flaps negative. Left lung: Lobes separate easily. Surface pale; mottled. Crepitates throughout. Slight anthracosis. On section dry; yield small amount of blood on pressure, less in upper lobe. Lower lobe more fluid and blood and lower portion more firm in consistency. Right lung: Darker on surface; pleura more congested; scattered areas which do not crepitate. Lower lobe is solid and crepitates in upper part of the lower lobe. More blood exudes than from left. On the surface are occasional yellow-white spots which on section are discrete in outline and yield a thick, yellow fluid. Lower lobe: Solid; on section two-thirds is airless and the spaces are filled with creamy

mucoid thick fluid. Bronchial glands: Very edematous; enlarged; slight pigmentation.

*Abdomen.* Peritoneum: Parietal peritoneum shows numerous white spots. At upper pole of wound site was a walled-off area which, when opened, let out a thick, creamy, mucoid fluid, recognized in the gross as pus. Tissues separated at wound site and a handful of clot scraped out. Area of clot and exudate extends over fundus of stomach, clear to esophageal junction. Spleen: Removed previously and in its site blood clots and adhesions of surrounding organs; at site of attachment of spleen the splenic mesentery is drawn up in a knot and still held in place by ligatures not absorbed. Left adrenal: Normal. Left kidney and ureter: Ureter not dilated; perinephritic fat scant in amount; fibrous capsule strips easily; surface smooth; stellate veins moderately distinct. Right adrenal: Normal. Right kidney and ureter: Ureter not dilated; surface smooth; capsule easily stripped; on section, bleeds easily. Duodenum: Admits thumb with ease. Bile passages: No obstruction; on pressure, *very* pale bile escapes. Pancreas: Tail of pancreas adherent to parietal peritoneum. Inguinal and cervical lymph glands were removed; not visibly enlarged.

MICROSCOPIC FINDINGS. Heart: Moderate cloudy swelling with some fatty degeneration.

Lungs: Purulent bronchopneumonia and metastatic abscess. Fibrinopurulent pleurisy.

Liver: Diffuse fatty degeneration. Marked pigmentation of liver cells which consists of bilirubin and hemosiderin. There is also a progressive fibrosis beginning in the islands of Glisson and ramifying between the hepatic cords. The change is almost identical to that found in the lymph glands. The tissue consists of fibroblasts, large endothelial cells, plasma cells, polymorphonuclears, and multinucleated endothelial giant cells.

Spleen: The splenic pulp is almost obliterated by a progressive fibrotic process which varies from an early stage with many fibroblasts to a later stage in which there are very few cellular elements. Intermingled with the fibroblasts are many plasma cells and multinucleated giant cells. Only an occasional Malpighian body is found, which in most cases consists of an artery almost obliterated by proliferative change, while the accompanying lymphocytes are few in number or are replaced by fibroblasts. That the process is quite an old one is shown by the many large areas of anemic necrosis generally diffused throughout the splenic substance. They are surrounded by a great collection of blood pigment giving an intense iron reaction.

Kidney: Generalized cloudy swelling which is more marked in some areas than others. Marked medullary congestion which is also present around the convoluted tubules and glomeruli. At the periphery of these areas the epithelium of the tubules shows a

heavy deposit of dark-brown to black granules of pigment of varying size.

Adrenal: Marked cloudy swelling; fatty degeneration; fibrosis and hemorrhage.

Thyroid: Negative.

The cervical lymph glands show slight lymphoid hyperplasia. The inguinal glands show very intense lymphoid hyperplasia, endothelial hyperplasia, great increase in stroma, multinucleated endothelial giant cells but no eosinophiles. The bronchial and retroperitoneal nodes show nearly the same changes, but the fibrosis is more extreme and the lymphoid changes are not so marked. There are many giant cells.

CRITICAL ANALYSIS. An analysis of this case shows that we have a chain of evidence entirely adequate for establishing the anomalous origin of this case of Hodgkin's disease.

1. I wish to lay stress on the fact that at no time in the patient's history has there been any noticeable enlargement of the cervical glands. This is an exceedingly pertinent fact, and in itself is almost conclusive evidence that we must look elsewhere for the origin of the condition.

2. As further evidence for the anomalous origin, we have the patient's first definite symptoms beginning with pain in the left hypochondrium, accompanied by chills and fever. At about the same time, the menstrual flow which had been normal for five years gave place to a vicarious epistaxis. Six months later a cold seemed to aggravate the pain in the left hypochondrium, after which she developed a persistent cough which lasted until her death. This symptom probably corresponded to the involvement of the bronchial glands.

3. Of the lymphatic structures involved by far the most advanced pathological changes were found in the spleen. The practical obliteration of the lymphoid tissue of the splenic pulp by the intense proliferation of the hyalin connective tissue and the many areas of anemic necrosis bore adequate testimony to the age of the condition.

4. The atrophy of the liver, with the extension of the typical Hodgkin's changes into its lymphatics, is further evidence that the splenic changes are very old.

The lack of involvement in most of the nodes in the upper extremities, coupled with the progressive involvement in the other nodes culminating with the very old changes in the spleen, as well as the fact that the events in the clinical history are a reciprocal to this sequence complete the chain of positive evidence that is necessary to establish the origin of the condition in this case.

Wade<sup>5</sup> reports a case the origin of which he interprets to be in the spleen. An abridgement of the findings follow: A farmer,

<sup>5</sup> Jour. Med. Research, 1913, xii.

aged fifty-five years, had had several attacks of malaria during his youth. Following a severe cold he developed pain under the left costal margin. In the several months which succeeded the pain moved gradually from this site to the umbilicus. Intermittent chills, fever, and night sweats were a prominent feature. For eight years previous to the attack, which eventuated in operation, the patient suffered from a pain in the right lumbar region. It was learned that he died two years after the operation; nothing more of the subsequent history was learned, nor was any autopsy obtained. An enlarged spleen was removed which showed the picture of Hodgkin's disease. Fibrotic changes were the most prominent, although no areas of necrosis, caseation, or calcification were found. No enlarged abdominal glands were noted at the operation. There was no superficial glandular enlargement. He concludes:

"That the spleen was the original site in the case herein presented may be denied on the ground of incomplete assurance of the absence of a focus elsewhere. It is true that without an autopsy at or about the time of operation, this could not be absolutely established, but it would seem that a consideration of the clinical history and of the operation and the microscopic findings indicate definitely that the process arose in this organ."

On physical examination the chest was negative and no superficial glands had been noted. Again, in his conclusions, he says:

"In view of our ignorance of the etiology of the condition, and of the fact that the process occasionally arises in other deep-seated lymphadenoid tissues, the possibility of a splenic origin cannot be denied. Since in this case there was at no time any enlargement of the superficial lymph glands, nor was there evidence of any lymphatic hyperplasia within the mediastinum or abdominal cavity, and since the disease was of long standing in the spleen as evidenced by the gross and histopathological appearance, it should be considered one of primary splenic Hodgkin's disease."

Symmer's case was that of a girl, aged eighteen years, with splenomegaly, who three years before her death from splenectomy passed clots of blood from the bowel and had a chronic relapsing fever. The spleen macroscopically and microscopically showed evidences of Hodgkin's disease, but no place in the description can I find evidence that the changes in the spleen were older than those in the lymph glands. The description states that "no areas of necrosis were found," and the changes in the lymph glands are not recorded because no autopsy was obtainable. He states that at the operation it was not noticed that the abdominal glands were affected, but this statement may also be difficult to prove without the aid of the microscope. He merely states that in his opinion the case represents one of primary splenic Hodgkin's dis-

case, and that he has not been able to find an exactly similar case in the literature.

A review of these cases show that they both fall in the same category, viz., the conjectural. It is true that they are both very suggestive, but the autopsy evidence which makes it possible to unequivocally demonstrate their contention is lacking. In Wade's analysis of his own case he admits that its origin in a focus elsewhere cannot be absolutely disproved without an autopsy, but believes that the case should be called a primary splenic involvement, particularly from lack of evidence of glandular involvement elsewhere, from the clinical history and from the exploratory results of the operation.

When the splenic origin of this condition is so much in doubt the assumption of lack of involvement of all lymphatic nodes on merely gross examination would seem to be taking too much for granted. As the chest was not opened, there is a dearth of evidence regarding the bronchial nodes, and in light of the present theories concerning etiology these nodes would naturally be next in order of involvement. It is a fact not generally recognized that one may have moderate enlargement of glands in one location, which may gradually subside, at which time the progress is usually active elsewhere. This circumstance, coupled with the fact that the inguinal glands in my case, showed moderately-advanced changes, although they were not abnormally palpable, would seem to seriously question the value of Wade's evidence that the lymphatic nodes in his case were not involved.

Another point regarding the clinical history, which he says points very strongly to primary splenic Hodgkin's: "The patient has given no other symptom for years but a pain in the region of the spleen." For eight years before the pain started under the left costal margin the patient suffered from pain in the left lumbar region.

A history of probable splenic trouble covering that length of time with no glandular involvement points much more strongly to a Gaucher type of splenomegaly than to Hodgkin's disease, which does not run such a prolonged course as the former. Under such circumstances I should think that it would be quite necessary to differentiate this condition. The microscopic picture is usually definite, but it must be borne in mind that these changes were superimposed on an old malarial spleen, which might seriously complicate the microscopic picture, especially since fibrosis was the predominating feature.

**CONCLUSIONS.** I am able to find no case in the literature which can be demonstrated to have had its origin in the spleen. The cases of Wade and Symmers are suggestive, but the absence of a complete autopsy render the evidence inconclusive.

I believe that in the case which we have reported we have all

the evidence necessary to demonstrate our contention. The entire clinical history covering a period of not over two years, the lymphatic glandular involvement of chest, abdomen, and inguinal regions, all showing changes decidedly younger than those in the spleen, complete a chain of evidence which is entirely adequate.

## RESULTS WITH CHOLESTERINIZED ANTIGENS IN NON-SYPHILITIC SERA.

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AND

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THAT additions of cholesterol to alcoholic extracts used as antigens in the Wassermann reaction increase the delicacy of the test is well established. As small an amount as 0.0125 gram per 100 c.c. of extract sharpens the end reaction.<sup>1</sup>

The specificity of cholesterolized antigens is questioned by many observers. It may be stated that even with those obtaining the best results, certain cases are reported as giving positive reactions which are questionably luetic. These questionable cases and those clinically non-syphilitic cases reported as giving positive reactions can not be placed into definite groups as can those which give non-specific reactions with the non-cholesterinized alcoholic extracts. Therefore, the clinical interpretation of positive results obtained with cholesterolized antigens must be slightly guarded.

Because of this an attempt has been made to find what amounts of cholesterol may be added to an alcoholic extract without decreasing its specificity as an antigen.

Three alcoholic extracts were used: two the livers of luetic feti and one of guinea-pig hearts. The liver extracts were prepared by shaking the finely chopped liver with ten parts of absolute alcohol for four hours on each of three days, placing in the incubator at 38° C. in the interim, decanting, and preserving on ice. The guinea-pig heart extract was made by placing one to two hearts into 500 c.c. of absolute alcohol every week for a period of six months.

The cholesterol additions were made by weighing into a 50 c.c.

<sup>1</sup>Loc. cit.



volumetric flask, then adding the alcoholic extract and placing in the incubator at 38° C. In two to four hours frequent shaking brought about complete solution of the cholesterolin.

The technic of titration for the anticomplementary amounts of the extracts and the Wassermann system employed were that of Citron as outlined by Garbat.<sup>2</sup>

In order to compare the cholesterolinized with the plain alcoholic extract from which it had been prepared, reactions were run simultaneously on all sera with both types of antigens.

The alcoholic extracts of livers are designated as "LL" and "VL," and of guinea-pig heart as "GP." The cholesterolin additions are designated as "CX," "CA<sub>1</sub>," "CA," "A," and "B."

Readings are designated as + + + +, + + +, + +, or +, depending upon the degree of inhibition of hemolysis. + + mean a positive reaction, the second antigen tube being hemolyzed, but the first showing complete inhibition of hemolysis.

For brevity + reactions are considered as negative, since in this clinic such reactions are considered as of no value in diagnosis.

Extract "LL" was compared with "CA<sub>1</sub>," containing 0.0248 gram of cholesterolin per 100 c.c., and "CA," containing 0.0496 gram, in 51 sera; 48 of these were negative with all three antigens. Three cases of syphilis were + with "LL" and "CA<sub>1</sub>," but + + with "CA."

"LL" and "CA<sub>1</sub>" were compared in 163 sera. Of these 140 were negative and 15 positive, with both types of antigens. Three cases of lues were negative with "LL" and + + with "CA<sub>1</sub>." Two cases were + with "LL" and + + with "CA<sub>1</sub>." Repetition of the reaction in the same sera twenty-four hours later gave + with both "LL" and "CA<sub>1</sub>." These two cases were clinically non-syphilitic. The diagnoses were neurasthenia and gonorrheal spur.

Extract "VL" was compared with the cholesterolin additions "CX," containing 0.0125 gram, "CA<sub>1</sub>," 0.0251 gram, and "CA," 0.0502 gram of cholesterolin per 100 c.c. of extract "VL."

With "VL" and "CX" agreement was obtained in 12 negative and 15 positive sera. The serum of a case of eczema clinically free from syphilis was negative with "VL," but + + with "CX." The same serum one week later was negative with both "VL" and "CX."

Agreement was obtained with "VL" and "CA" in 33 non-syphilitic sera. "CA" was positive and "VL" negative in the sera of 2 syphilitic cases.

"VL," "CA<sub>1</sub>," "CA" were compared in 14 sera. There were 12 negative agreements. One case of lues was + with "VL" and "CA<sub>1</sub>," but + + with "CA." A case of inguinal hernia which was

<sup>2</sup> Immunity, Citron and Garbat, Philadelphia.

clinically free from lues was + with "VL" and "CA<sub>1</sub>" but ++ with "CA."

"VL," "CX," "CA<sub>1</sub>," and "CA" were compared in 41 negative sera. Negative agreement was obtained in 40 of these. A case of pseudoleukemia vera which was clinically free from syphilis gave ++ with "CX" but was negative with the other three antigens.

Extract "VL" was compared with "B" containing 0.0996 gram of cholesterol per 100 c.c. in 89 sera; 62 negative and 21 positive agreements were obtained. In 6 cases of lues "VL" was negative but "B" ++.

Extract "GP" was compared with "A" containing 0.101 gram of cholesterol per 100 c.c. in 288 sera; 239 negative and 37 positive agreements were obtained. In 6 cases of syphilis "A" was ++ but "GP" negative; 6 cases without evidences of syphilis gave ++ with "A" and negative reactions with "GP." On immediate repetition of the reactions with the same sera and the same reagents which were used in the primary test 5 of these sera gave + results. The diagnoses in these cases were rheumatic endocarditis, optic atrophy (the cerebrospinal fluid was negative for pleocytosis, globulin, and Wassermann), lobar pneumonia, and two of pregnancy.

DISCUSSION AND SUMMARY. The above results were obtained in 658 sera of 501 cases. All of these cases were house patients and were subjected to the usual thorough routine study. Where questionable results were obtained with the cholesterolized extracts, special care was taken to detect evidences of syphilis. Negative sera were largely used, positive sera being used only in number enough to show the value of the experimental antigen.

Non-specific reactions have been obtained with antigens representing additions of 0.0125, 0.0248, 0.0496, 0.0502, and 0.0996 gram of cholesterol to 100 c.c. of the alcoholic extract of syphilitic livers; also, with an addition of 0.101 gram of cholesterol to 100 c.c. of the alcoholic extract of guinea-pig hearts. The percentage of error has been 1.97 per cent.

That ++ of one day may be + the next or a week later, as occurred above, may be explained by changes in the serum, the strength of the complement, or by differences in the suspension of corpuscles. But when a serum is ++ one hour and + the next hour an explanation is not so obvious. The technic was so carefully controlled throughout that it would not seem possible to account for the discrepancy on the grounds of technical error. It has been noted from time to time that + sera often vary in their degree of inhibition of hemolysis with the same reagents. Not infrequently the degree of inhibition of hemolysis with + non-luetic sera was greater with the cholesterolized extract than with the alcoholic extract. In eight such sera this inhibition was particularly marked, the cholesterolized extract giving almost a positive (++) reaction.

It is possible that this increase in the anticomplementary power produced by the cholesterinized extracts when coupled with the variability in the inhibitory qualities of weakly positive sera manifested itself in the cases in question in ++ the one time and + the other.

Two sources of error have been guarded against throughout: error in technic and error in diagnosis. Care and experience tend to rule out the former. As regards the latter error every measure was taken, except the use of luetin, to determine the presence or absence of syphilitic taint in those cases whose sera gave questionable reactions.

The conclusion is drawn that cholesterin additions in the amounts above employed render the alcoholic extract more sensitive but somewhat less specific, and therefore of questionable value in the diagnosis of syphilis.

## DIAGNOSIS, SYMPTOMATOLOGY, AND THERAPY OF DILATATION ANEURYSMS OF THE DESCENDING THORACIC AORTA.

BY SELIAN NEUHOF, M.D.,

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A CENTURY ago Hodgson<sup>1</sup> made the fundamental distinction between sacculated and "dilatation aneurysms." He defined the latter as a "preternatural permanent enlargement of the cavity of an artery;" the former is a definite protusion of only one side of its wall and may include a small or large part of the arterial caliber. This distinction seems to be of clinical importance in aortal disease. The French still apply the term "Maladie de Hodgson" to aneurysmal dilatations of the aorta associated with valvular insufficiency. Aortitis of the ascending and transverse aorta is now known to be of luetic origin in the great majority of instances.<sup>2 3</sup> The pathology and mechanism of aneurysmal dilatations of these parts of the aorta have been described in detail by Thoma,<sup>4</sup> who had studied ninety-two cases. He ascribes their fundamental cause to lessened resistance of the arterial walls, and categorically states that "such weakened condition is not found in the descending thoracic aorta,"<sup>5</sup> which showed no change macro-

<sup>1</sup> Engravings of Diseases of the Arteries, 1815; Treatment of Diseases of the Arteries and Veins, 1815.

<sup>2</sup> Gruber: Ueber d. Doehle-Hellerische Aortitis.

<sup>3</sup> F. Kraus, Deutsch med. Wehnschr., 1911, xi, 577.

<sup>4</sup> Virchows Archiv, 1888, cxi, 89.

<sup>5</sup> "Dass die Bildung der spindelförmigen Aneurismen vor allem eine Verminderung der Widerstandsfähigkeit der Gefässwände zur Voraussetzung habe und dass hier diese Voraussetzung fuer absteigende Brustorta nicht erfüllt sei."

scopically. The pathological process in dilatations of the first and second parts of the aorta consists of a mesaortitis, with perivascular infiltrations of the vasa-vasorum, small-celled or granulomatous infiltration in areas of the media, and splitting and destruction of the muscular and elastic tissue layers.<sup>6,7</sup> Diffuse dilatation of the entire thoracic aorta from its root to the diaphragm is occasionally seen. The writer has observed two such cases: one was an autopsy finding and included severe myocarditis and coronary sclerosis, and the other he was able to diagnose by physical signs in conjunction with fluoroscopy.

Recent reports of aortitis are almost entirely confined to disease of the ascending or transverse aorta<sup>8</sup> with fragmentary or no reference to the descending thoracic aorta. McCrae,<sup>9</sup> Allbutt,<sup>10</sup> Osler,<sup>11</sup> and others consider aneurysmal dilatation of the descending thoracic aorta extremely infrequent, a statement apparently based upon postmortem findings, for no symptomatology is mentioned nor had a clinical diagnosis been made. The object of this paper is to indicate through illustrative cases the comparative frequency, diagnosis, symptomatology, and therapy of aneurysmal dilatations of the descending thoracic aorta and to present its claim to a clinical entity.

CASE I.—G. G., male, aged sixty-seven years, had never been seriously ill previous to his present complaint. He had been a heavy smoker and had suffered from a venereal infection forty years ago, for which he had received many subcutaneous injections, presumably of mercury. His present illness began two years ago with exceedingly mild symptoms: very slight precordial pains when lying on the left side and slight dyspnea upon climbing stairs. Upon examination the patient looked well preserved, the carotid pulsation on both sides was somewhat exaggerated, and there was a ring of small dilated capillaries on the lower part of the chest. The cardiac thrust at the apex and the systolic impact at the right base felt somewhat exaggerated. The cardiac area seemed normal to percussion. At the base there was a double murmur, a rough systolic and a softer diastolic, which was transmitted and best heard to the left of the middle third of the sternum; a definite sensation of heaving impulse was imparted to the examining hand placed over the same area. Similar but fainter murmurs were heard at the apex. Both radial pulses were alike: the average systolic blood pressure was 170 mm., the diastolic, 70. The neurological status and the other organs were normal. There was slight pretibial edema, which lasted one week. The Wassermann reaction was

<sup>6</sup> Osler's System of Medicine, iv, 457.

<sup>7</sup> Adams and Nicholls, Principles of Pathology, 2d edition, 178.

<sup>8</sup> Longcope, Arch. Int. Med., 1913, xi, 1.

<sup>9</sup> AMER. JOUR. MED. SCI., 1910, cxi, 169.

<sup>10</sup> System of Medicine, vi, 658.

<sup>11</sup> Ibid., iv, 457.

negative. The roentgenogram (Fig. 1) and orthodiascopic tracing showed a long fusiform dilatation of the entire descending thoracic aorta. The electrocardiogram, negative R, in Lead 3, showed evidence of left ventricular preponderance.<sup>12 13</sup> Treatment consisted of one salvarsan and many mercurial injections; iodide of potash in moderate doses was administered in alternate periods of two weeks. Tincture of digitalis was given for one week until



FIG. 1.—Roentgenogram of Case I. Fusiform dilatation of the thoracic aorta.

the edema of the legs disappeared. The patient has been under observation for two years; he has been quite comfortable, with no pains for over one year; the physical signs along the middle third of the sternum have markedly diminished.

<sup>12</sup> Lewis, *Heart*, 1914, v, 367.

<sup>13</sup> Einthoven, *Archiv f. die gesammte Physiologie*, 1908, cxxii, 517.

CASE II. A. K., female, aged forty-seven years, married sixteen years, had never been pregnant. Prior to the present illness she had always felt well. Two years ago she complained of dyspnea on exertion and of nocturnal palpitation accompanied by pain in the lower precordium. She lost about forty pounds since her illness began. One week before admission to the Lebanon Hospital her legs became edematous. The patient was emaciated, the right pupil was somewhat larger than the left, both reacted sluggishly to



FIG. 2. Roentgenogram of Case II. Fusiform dilatation of the thoracic aorta.

light, but normally to accommodation; the knee reflexes were slow; Rhomberg's symptom was absent. The patient was dyspneic even when at rest. There was vigorous, visible carotid and jugular pulsation; the aortic thrust could be plainly felt by pressing the tip of the finger behind the manubrium. By placing the eye on a level with the patient's chest, two distinct areas of impact were discernible; one corresponding to the apical region and the other to an area slightly to the left of the lower half of the sternum. The latter impact was also palpable by insinuating the fingers in the lower

left intercostal spaces and also by placing the bell of the stethoscope over this area during the course of a routine clinical examination. There was no precordial tenderness to pressure. The apex was felt most distinctly in the sixth interspace 14 cm. from the mid-sternal line. Over the base, and particularly to the left of the middle sternal border, there was a rough systolic murmur and a somewhat accentuated second sound which merged into a soft murmur occupying the entire diastole. Friction sounds probably indicative of dry pericarditis were present at the base and apex. There was slight edema of the legs. The Wassermann reaction was negative upon first examination; some months later it became positive. The systolic blood-pressure ranged between 200 and 180 mm., the diastolic between 100 and 40 mm.; the pressure in both arteries was equal; the urine was normal. The roentgenogram (Fig. 2) showed fusiform aneurysmal dilatation of the entire descending thoracic aorta; orthodiascopic examination corroborated this finding. The electrocardiogram presented evidence of left ventricular preponderance. The patient refused treatment; she has since reëntered the hospital, with signs of severe cardiac failure. She subsequently received iodide of potash and mercurial injections, with marked improvement.

CASE III.—L. J., male, aged fifty-three years, laborer, married; denied all venereal infection. Three and one-half years ago he developed substernal pains and dyspnea upon walking. One year ago he was compelled to stop work because of the frequency and severity of these attacks. The pains usually radiated to both sides of the chest, shoulders, lower jaw, and right side of the head. During the last few months he frequently had pharyngeal spasms upon attempting to swallow fluids, so that the latter were occasionally regurgitated through the nose. There were no gastric symptoms. The patient looked florid and well nourished; there was no dyspnea when at rest. Upon admission to the Lebanon Hospital the patient's right pulse was much smaller than the left; there were no abnormal carotid or jugular pulsations. The apex beat was best heard in the fifth interspace, 7 cm. from the midsternal line. On auscultation the first sound at the apex was scarcely audible; the second sound was normal. The first sound at the right base could not be heard; the second sound was normal; both were distinctly heard to the left of the middle third of the sternum, the first sound being normal in intensity and the second somewhat accentuated. There was no edema of the legs. Examination of the other organs revealed nothing abnormal. The Wassermann test was negative. An interesting phenomenon was the fact that intermittently for several weeks the right radial was smaller than the left, a difference which sometimes amounted to 10 mm. of mercury in the systolic brachial pressures; these inequalities had no relation to the symptoms. The roentgenogram showed a distinct

somewhat tubular shadow behind the hypertrophied left ventricle. With the orthodiascope the shadow of the dilated descending aorta could be faintly seen through the upper ventricular shadow. The electrocardiogram presented the usual evidence of left ventricular preponderance. The patient was given three injections of salvarsan intravenously and numerous mercurial injections combined with iodide of potash. The pains and pharyngeal spasms

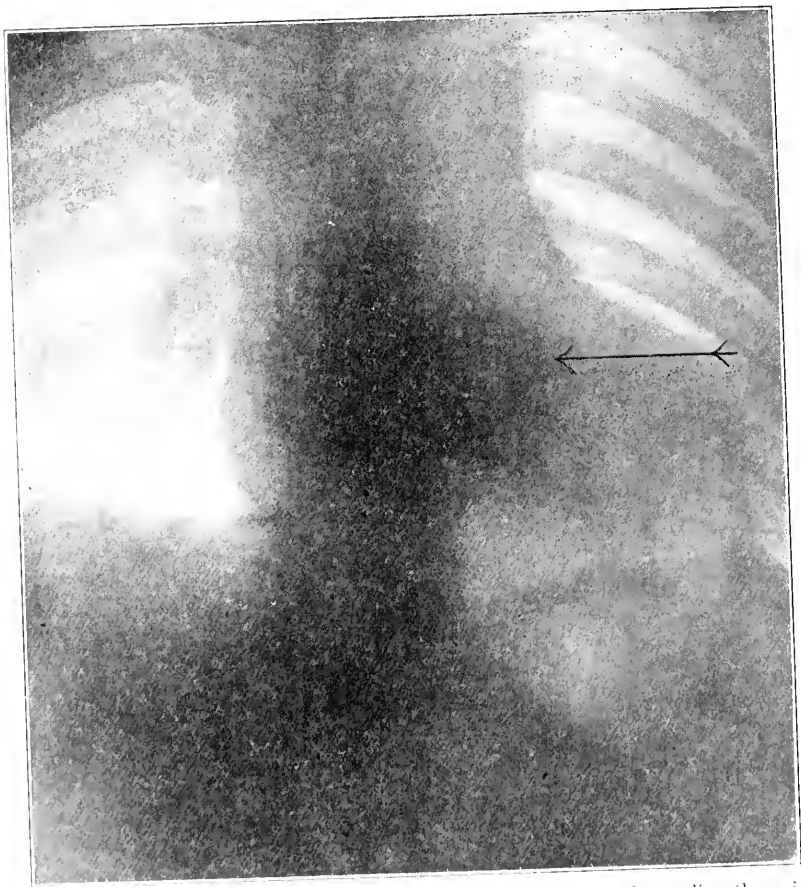


FIG. 3. Roentgenogram of Case IV. Dilatation of part of the descending thoracic aorta.

gradually subsided; the pulse inequalities became only occasionally noticeable, and finally disappeared entirely; the abnormal physical signs to the left of the sternum markedly diminished. He returned to work; his present complaint consists of slight occasional sub-sternal pain on walking.

CASE IV.—R. S., male, aged thirty-eight years, a vigorous and healthy looking man, complained during the last six months of



slight dyspnea upon climbing stairs, but none when at rest. He was a heavy cigar smoker. He had gonorrhea twenty years ago and denied any other illness. The blood-pressure was normal. There was vigorous carotid pulsation at the root of the neck. There was no pain on precordial pressure. The apex beat was strong, and was felt most plainly in the fourth interspace, 11 cm. from the midsternal line. A soft systolic murmur was heard at the

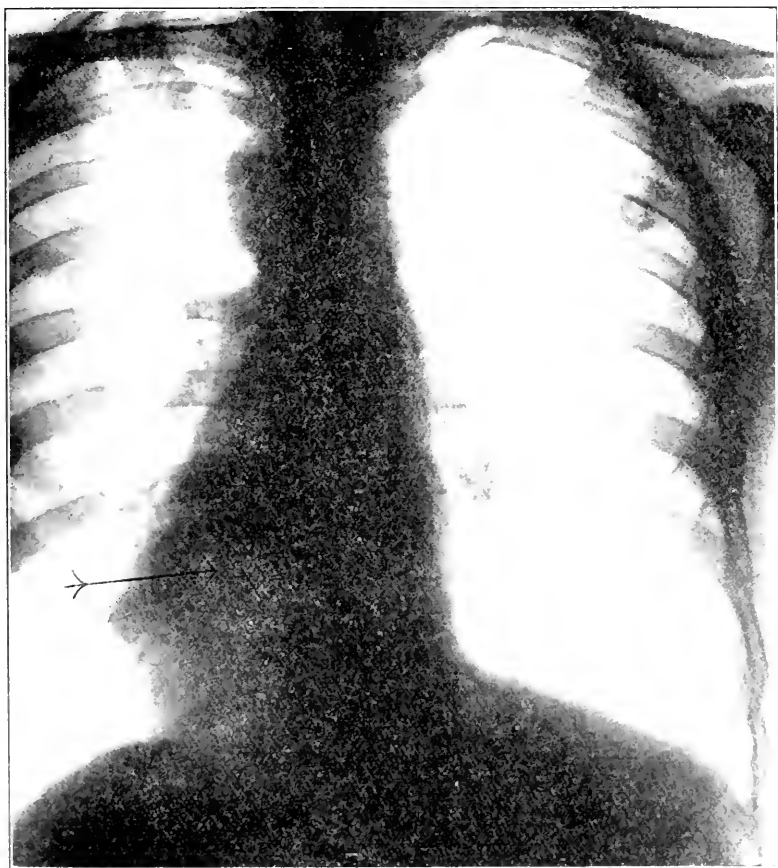


FIG. 4.—Roentgenogram of Case VI. Fusiform dilatation of the descending thoracic aorta.

apex. At the base the first sound was impure, the second was not accentuated, but was prolonged and somewhat liquid in character and occupied the whole of the diastole; these abnormal sounds were heard loudest and most distinctly along the middle left sternal border. The eye placed on the level with the chest could discern a slight systolic heave over the latter area, which was apparently distinct from that at the apex. The other organs were normal.

The Wassermann reaction was negative. The roentgenogram (Fig. 3) showed dilatation of the upper part of the thoracic aorta, the latter being visible as a somewhat denser shadow behind the ventricles. The orthodiascope confirmed this finding. The electrocardiogram was normal. The patient was given salvarsan, 0.3 gm. intravenously, and many bichloride injections combined with iodide of potash. The dyspnea has entirely disappeared; the abnormal sounds at the base and left sternum are much less pronounced than at the first examination.

CASE V.—M. B., male, aged fifty-three years, entered the hospital in the surgical service of a colleague but did not come under the writer's observation. The history was that of an esophageal stricture situated in the midthoracic region. The aneurysmal dilatation was discovered in making a routine roentgenographic examination of the chest. The stricture was presumed to be due to the pressure of the dilated aorta. The Wassermann test had not been done. The patient passed from observation. The case is included here because the roentgenogram is typical of aneurysmal dilatation of the descending aorta (Fig. 4).

SYMPTOMATOLOGY. Sharp, continuous, gnawing pains, such as those often associated with sacculated aneurysm, are not prominent features of the dilated descending aorta. When present, substernal pains or those referred to different parts of the chest, neck, jaws, or head are most apt to occur upon exercise. It is difficult to state the exact etiology of these pains. It does not appear probable that they are the direct effect of pressure of the dilated aorta upon the surrounding structures, esophagus, ribs, dorsal vertebra, intercostal nerves, etc. In one case (Case V) the cause of the pains may have been due to esophageal stricture, not to aortal pressure; in a case of rheumatic mitral stenosis under the writer's observation that came to autopsy a luetic ulcer of the esophagus which had been diagnosed during life was found to be the cause of the precordial pains. The elongated contour of the aneurysmal dilatation would in itself militate against a pressure and finally an erosive tendency. The rich nerve and ganglionic plexus surrounding the root of the aorta, and the nerve fibers and isolated cells which have been described in the connective tissue of the middle coat of the aorta<sup>14</sup> may tend to explain how various grades of inflammation in the aorta and how differences of aortal pressure and dilatability may give rise to these referred pains. In addition, periaortitic inflammation with possible involvement of the neighboring nerve structures may also cause neuralgia. Such nerve involvement has been found in dilatations of the ascending aorta and arch.<sup>15</sup> The assumption of inflammatory exacerbations within or without the aorta is partly corroborated by the occasional rapid subsidence of

<sup>14</sup> Manoélian, *Annales de L'Institut Pasteur*, June, 1911.

<sup>15</sup> Thoma, *Virchows Archiv*, 1888, cxi, 89.

the pains following salvarsan injections. This result is probably ascribable to control of these exacerbations, though Vaquez and Laubry<sup>16</sup> and Vaquez and Bordet<sup>17</sup> claim that there is sometimes a reduction in the size of sacculated aneurysms after several salvarsan injections. The writer has not yet been able to determine any difference in the size of the dilated descending aorta as the result of therapy. In addition to the aortal disease it must be remembered that accompanying coronary sclerosis and myocarditis may in themselves produce cardiac pains.

Another group of symptoms is that due to cardiac decompensation. This is not necessarily a marked clinical feature; in fact, in three of the cases it consisted only of slight dyspnea upon exertion. Its presence may be due to accompanying cardiovascular disease rather than to the aortal dilatation itself. Edema is usually slight and confined to the legs; it is extreme in neglected cases alone or late in the disease. Dyspnea is of the usual cardiac type; it is generally most marked on exertion, though it may be continuous in severe cases of cardiac failure. Left ventricular hypertrophy of varying degrees is usually present. The heart is occasionally tremendously hypertrophied before cardiac failure sets in, a fact in itself highly suggestive of cardiac lues.

**DIAGNOSIS.** The diagnostic criteria of aneurysmal dilatation of the arch and ascending aorta have frequently been emphasized,<sup>18 19</sup> particularly the rough systolic murmur and the accentuated, sometimes ringing second sound at the right base. In dilatation of the descending aorta abnormal sounds in typical instances are best heard at the left sternal border at its middle third or from the third left intercostal space to the ensiform. This latter area of propagation is somewhat similar to that occasionally found in valvular aortic regurgitation. The signs outlined, the impact area, the rough first and accentuated or liquid second sounds, will usually serve as differential guides. There is usually a rough systolic murmur over the dilated aortal area; the second sound has a liquid rather than an accentuated tone, and is prolonged so as to occupy the entire diastole or is followed by a diastolic murmur of varying intensity. Though this double murmur is the rule the only auscultatory difference may be a slightly impure first and a somewhat accentuated second sound. By placing the eye upon a level with the patient's chest a distinct heaving area distinguishable from that at the apex, and occupying the lower left sternal intercostal spaces, can often be detected. A sensation of impact is also given to the bell of the stethoscope when, during the usual clinical examination, it is placed over this area. This impact sensation is par-

<sup>16</sup> *Archiv. d. maladies du cœur*, 1912, v, 561.

<sup>17</sup> *Le Cœur et L'Aorte*.

<sup>18</sup> Held, *Medical Record*, 1913, lxxiv, 105.

<sup>19</sup> Longcope, *Arch. Int. Med.*, 1913, xi, 1.

ticularly well detected by snugly insinuating two or three fingers in the left middle interspaces near the sternum and then flattening out the fingers so that they rest well applied to the chest wall of this region. Occasionally a systolic thrill is also palpable. All these signs are made more evident by having the patient hold his breath at the end of expiration. Occasionally a difference in the time of thrust between the apical and left intercostal area may be noticeable by placing one finger over the apex and the other over the left sternal border; since, however, this difference, physiologically, is 0.07 second, it may be impossible to distinguish it by palpation. Another method is to use a differential stethoscope, *i. e.*, an ordinary pair of ear tubes arranged with two bells, one over the apex and the other over the dilated aorta. When the murmurs are not too loud the difference in time impact may be thus determined. The writer has also attempted to establish this difference by placing two receiving cups of a polygraph over these areas and noting the time of arrival of the thrusts upon the polygraphic paper, but the results were inconclusive.

It is important to distinguish the aortal impacts to the left of the sternum from those found in patients with marked left ventricular hypertrophy or in healthy individuals with overacting hearts and thin chest walls, but the auscultatory signs above described are then absent. Though there are many refinements of percussion methods used in the attempt to delicately outline the dilated arch and ascending aorta, for example, threshold and auscultatory percussion, their value in dilatation of the descending aorta seems exceedingly problematical because the latter is deep seated and most of the enlarged area is situated behind the ventricles. An examination of the posterior chest wall also fails to reveal any difference from the normal physical signs. In three of the reported cases in whom a correct tentative diagnosis was made before fluoroscopy, all methods of percussion failed to reveal enlargement of the descending aorta. To clinch the diagnosis, Roentgen-ray examinations by means of the fluoroscope or roentgenograms are absolutely essential. As in examination for suspected disease of other portions of the aorta, the patient should be fluoroscoped in several lateral positions. Fluoroscopy must be carefully practised in order to reveal and distinguish the darker silhouette of the dilated descending aorta behind the left ventricle. Roentgen-ray plates must also be carefully scrutinized for the same reason. It is important in this connection to indicate the differences in shadow areas between orthodiascopic fluoroscopy and roentgenograms of the heart and aorta. It has been the writer's experience that the former produces very little distortion in the size of the cardiac and aortal areas, because the Roentgen-ray tube and screen move together and thus rays approximately parallel reach the observer. In the roentgenogram, since the rays are divergent, there is

of necessity an increased photographic cardiac shadow. An example of such Roentgen-ray distortion came under the writer's observation. The roentgenogram showed a cardiac shadow which reached almost to the axillary line. At autopsy the heart was only moderately enlarged; a thick adherent pericardium precluded agonal cardiac dilatation as a cause for the distorted roentgenogram, which was taken shortly before death. Comparisons between the orthodiascopic tracings and roentgenograms occasionally showed marked discrepancies in the size of the dilated aorta and heart; this was specially noticeable in one of our cases. The reasons given tend to confirm the accuracy of the orthodiascope as the more exact method for delimiting the aorta and heart.

**THERAPY.** Treatment may be conveniently divided into three parts: that of the underlying disease, the decompensation, and the pains. The majority of cases of aortal disease is known to be of luetic origin, the Wassermann reaction being positive in most instances. Salvarsan was originally considered contraindicated by Ehrlich himself in cardiac lues because of the fear of overwhelming the system with spirochetes (Herxheimer reaction), but experience has shown that the drug judiciously administered is definitely indicated in this disease.<sup>20</sup> Three of the cases here reported were thus treated, with excellent results. The best routine procedure is the intravenous injection of 0.2 gm. of salvarsan every week until three doses have been given; then, if indicated, it may be repeated in 0.6 gm. doses a month or two apart. In the interim intramuscular injections of mercury about twice weekly should be given in conjunction with iodide of potash. If the luetic changes in the aorta are such that calcification and scar-tissue formation are extensive and the myocardium is the seat of advanced disease the treatment can be of little or no avail. The degree and extent of such pathological changes cannot be diagnosed accurately enough by our present methods, though Vaquez and Bordet<sup>21</sup> claim to have observed with the fluoroscope calcified areas in the ascending and transverse aorta and the diminution of these areas resulting from salvarsan injections. Since the treatment outlined is often efficacious and is followed by marked improvement the writer believes it should be carried out in all cases unless the patient is *in extremis*. Even if the Wassermann reaction be negative the same therapy should be instituted, because syphilis is the preponderatingly etiological factor of extensive aortitis, and because in any case salvarsan is not followed by serious results. Besides, a Wassermann reaction which upon the first examination is negative may later become positive even though no provocative injections had been given; this happened in Case II.

<sup>20</sup> Vaquez et Laubry, *Archiv. de mal. d. cœur*, 1912, v, 561.

<sup>21</sup> *Le Cœur et l'Aorte*.

Cardiac failure accompanying dilatation of the descending aorta requires the same treatment as that from other causes. A reliable preparation of digitalis should be given. The writer prefers the tincture administered undiluted in 15-drop doses t. i. d. If urgency demands it and very little or no digitalis had previously been given 1 c.c. of strophanthin may be slowly injected intravenously. The objection that digitalis in therapeutic doses raises blood-pressure has been sufficiently disproved by recent careful investigations.<sup>22 23</sup> Digitalis had no effect upon the blood-pressure in our cases; it was as often lowered as raised during its administration. Symptomatic treatment of the pains may occasionally require codein or morphin, but the pains are frequently relieved by the antiluetic treatment, which presumably acts by controlling the inflammatory exacerbations of aortitis and periaortitis.

**PROGNOSIS.** Dilatations of the descending aorta are frequently overlooked: in fact, except in the course of a routine Roentgen-ray examination of the chest its diagnosis by clinical methods has, to the writer's knowledge, never previously been made. If the patient seeks advice before severe decompensation sets in, and if then the condition be properly diagnosed and vigorous antiluetic treatment instituted, the patient may live in comparative comfort, for the aortal disease is an index of the general cardiovascular mischief rather than in itself the cause of cardiac failure. Of the three patients with slight symptoms who have been under observation for one year or more, two are clinically well and one is very much improved. The cardiac condition of the patient with the esophageal stenosis (Case V) is not known.

Cure in the sense of a return of the aorta to its normal state is impossible; but, as in other organs, the luetic disease may be arrested and controlled, and the heart and aorta, though somewhat crippled, be sufficiently restored to make the patient comfortable. Rupture of the dilated ascending and transverse aorta is extremely infrequent. Unless the luetic disease is severe and confined to a small area, this accident seems less likely to occur in the descending aorta because of its greater length and because the dilatation spreads over a larger area.

**RÉSUMÉ.** The Wassermann test was done in four of the five cases reported. It was positive in two and negative in two. One of the latter gave a definite history of luetic infection. Three cases (I, III, IV) had slight symptoms when treatment was begun; these were clinically cured. Case II, with severe heart failure, was much improved. In three cases (II, III, IV) the correct tentative diagnosis was made by the presence of an impact area to the left of the sternum at its middle third and by the localization of prominent murmurs over this area. Electrocardiograms were taken in

<sup>22</sup> Mackenzie, *Heart*, ii, 281.

<sup>23</sup> Pierce, *British Med. Jour.*, 1912, 689.

four cases; three showed complexes of left ventricular preponderance and the fourth was normal. The physical signs of all the cases were most marked when the symptoms—dyspnea, pain, or cardiac failure, were present; the signs became less with the patient's improvement.

In conclusion it may be stated that aneurysmal dilatation may be confined to the descending thoracic aorta alone; it may then occasion sufficiently definite physical signs to lead to its tentative diagnosis by the ordinary methods of clinical examination. The physical signs are most prominent to the left of the sternum at its middle third. Roentgen-ray investigation is indispensable for a positive diagnosis. The symptoms are often very slight. The disease may run a mild course, lasting many years. Intensive antiluetic treatment—salvarsan, mercury, and iodide of potash, is indicated in every case.

Cases II and III occurred in the service of Dr. Richard Stein, visiting physician to the Lebanon Hospital, to whom I am greatly indebted for the privilege of reporting these cases and for his interest in the work.

## **DIRECT BLOOD TRANSFUSION WITH THE KIMPTON-BROWN TUBES: A REPORT OF NINE CASES.**

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AND

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ON account of the general interest that has of late centered around blood transfusion by the methods of Kimpton and Brown,<sup>1</sup> Lewisohn<sup>2</sup> and others, we venture to report a small series of cases treated by the Kimpton-Brown method and using the tubes and technic as described by Mason.<sup>3</sup>

The urgent need of a simple and yet efficacious method of blood transfusion, particularly in emergencies, has long been felt. Special skill, combined with an intimate knowledge of the technic involved, place the end-to-end suture of vessels beyond the reach of the average surgeon. Therefore, we welcomed a method that could be used readily, with little preparation and no special skill on the part of the operator.

<sup>1</sup> Jour. Am. Med. Assn., July 12, 1913.

<sup>2</sup> Med. Rec., January 23, 1915; Surg., Gynec. and Obst., July, 1915.

<sup>3</sup> Surg., Gynec. and Obst., June, 1915.

Our experience with the Kimpton-Brown tubes has been very gratifying. We believe that the ease of execution, the lack of complications, and the immediate improvement following their use commends this method for use in any case in which blood is needed, although in our experience we found certain contra-indications to its use. When a general infection, such as septicemia or cholemia, is present, little can be expected by blood transfusion. In our cases of simple hemorrhage the best results were obtained, and this, of course, is the experience of all who have used any method of blood transfusion.

We have but two criticisms to offer concerning the Kimpton-Brown tube. One is, that whenever we used the large corks in the tubes, considerable difficulty and annoyance were encountered, because of a tendency for the cork to be forcibly ejected from the tube by the rise in pressure when the blood was being forced into the vein of the recipient. To re-sterilize the cork or to replace it with another consumed valuable time. We finally discarded the corks entirely and now use the palm of the gloved hand, placed tightly over the top of the tube. This works well and simplifies the technic somewhat. The other criticism would better be called a fault on our part rather than a condemnation of a point in the technic. We speak of the difficulty encountered in uniformly coating the tubes with paraffin and of keeping clear the lumen of the tip through which the blood enters and leaves. At first we found that the last drop of paraffin would invariably harden in the tip and prevent the entrance of the blood. To make the lumen of the tube of greater diameter seemed hazardous, as small veins are met with so often that it is imperative to have a tip that will enter easily the smallest vein. To overcome this difficulty we hit upon the following simple plan: We had about 200 c.c. of melted paraffin at hand. A part of this was poured in the tube, the palm of one hand covering the mouth of the tube and a finger over the tip, and the tube was rapidly rotated, causing the paraffin to come in contact with all parts of its walls. Then the paraffin was allowed to run from the tube while the hand bulb and rubber tube were quickly connected to the arm of the tube and air was forced in, keeping the palm of one hand tightly over the upper opening in the tube. This procedure caused all of the paraffin to be ejected and the air under pressure maintained a lumen in the tip until the paraffin had hardened. After using this slight variation we had no trouble whatsoever in rapidly carrying out the procedure.

Nine patients were given blood transfusion. Of the 9, 3 died, all of whom suffered from infection of one kind or another. The 6 cases that recovered were very satisfactory, inasmuch as all were practically moribund, and we felt their recovery was due entirely to their receiving blood transfusion. Moreover, the improvement in these cases was marked and rapid, and we could not but be



impressed by the sight of a gasping, dying patient, changing before our eyes, to a conscious, red-cheeked person.

The cases used were from the service of Dr. John B. Deaver, of the German Hospital, and we take this opportunity to thank him for the privilege of reporting this paper and for his never-failing interest and aid.

**CASE REPORTS.** **CASE I.**—H. E., female, aged fifty-eight years. Admitted September 13, 1915, with a clear history of gall-stone disease. Past medical history of no importance. The blood count, on admission, showed hemoglobin, 88; red blood cells, 5,030,000; white blood cells, 7650; coagulation time, eight minutes. Five days later at operation the gall-bladder and appendix were removed and the common duct was drained. Twenty-four hours after operation a moderate hemorrhage from the bowel occurred. The pulse rose to 156 and a blood count showed hemoglobin, 65; red blood cells, 4,160,000; white blood cells, 17,500. The patient became steadily weaker, the pulse varying from 140 to 160 per minute. Resort to intravenous infusion of saline and hypodermoclysis was of no avail. Ten days after operation the hemoglobin had dropped to 30 and the red cells to 1,000,000. The leukocytes now reached 28,000, with 83 per cent. polynuclears. At this time the patient was practically moribund: she was comatose and death seemed inevitable. It was decided to seek someone who would give blood for transfusion. A healthy son, aged twenty-eight years, acceded to our request. The usual technic was followed and something over 800 c.c. of blood were introduced into the vein of the patient, with surprising results. Immediately the patient became alert, the eyes brightened, and the face became flushed. She asked for water and food and her pulse became slower and of normal volume. Blood examination the following day showed hemoglobin, 40; red blood cells, 2,010,000; white blood cells, 26,050. No further hemorrhage occurred. The blood counts, which were taken daily for some time, showed a slow progressive improvement. When she was discharged, five weeks after admission, the hemoglobin was 47 and the red blood cells were 3,000,000. A suppurative parotitis delayed the convalescence somewhat. The patient felt strong and active. As to the cause of the hemorrhage we are uncertain, although it is probable that it was a toxic oozing from the large intestine. No difficulty was met with in the technic in this case. The donor showed little the wear of having lost almost a quart of blood, and was able to resume his work in two days.

**CASE II.**—J. D., male, aged thirty-two years. Admitted November 24, 1915, with a history of gall-stone disease. Three days later, at operation, the gall-bladder and appendix were removed and the common duct was drained. The morning following the operation it was noted that a considerable quantity of blood was

staining the dressings. Morphine and horse serum were given, but the bleeding increased alarmingly. The pulse rose to 166 and the patient looked deathly pale. The blood count on admission was hemoglobin, 83; red blood cells, 3,980,000; white blood cells, 8550. Just twenty-four hours after operation the patient was etherized, the wound reopened, and the gall-bladder fossa inspected for bleeding. However, none was found, so the wound was closed and the lower wound (McBurney incision) was reopened. On inspecting the viscera a general interstitial bleeding in the mesentery and omentum was found. A large amount of free blood was sponged out of the abdominal cavity and the wound was closed, leaving a glass tube in for drainage. While on the table the blood count was taken and showed hemoglobin, 27; red blood cells, 1,820,000; white blood cells, 24,550; polynuclears, 79 per cent. An attempt promptly made to obtain a donor for blood transfusion met with failure until twelve hours following the second operation. During this interval the bleeding had continued, large amounts being syringed from a glass drainage tube. After some persuasion a brother-in-law of the patient finally consented to act as donor. He was a large, strong man and showed no symptoms whatever after the withdrawal of over 650 c.c. of blood. Owing to a small bit of paraffin being dislodged by forcing in the cork in the tube, and causing an obstruction in the lumen of the tip, the first 200 c.c. of blood clotted and we were compelled to hastily coat a second tube, when no similar trouble ensued, and over 400 c.c. were introduced in the vein of the recipient. A rapid improvement in the patient's condition became at once apparent. The pulse slowed, the color became better, and the mind alert. During the following twelve hours the bleeding ceased entirely and the man continued to improve. The blood count rose, the hemoglobin was 54, and the red blood cells were 3,110,000. The patient still remains in the hospital and is making a satisfactory recovery. On December 11, 1915, the blood count showed hemoglobin 57; and the red blood cells 3,120,000. No further bleeding has occurred.

CASE III. — L. V., female, aged twenty-seven years. Admitted November 20, 1915, with a most interesting history. Four days previously she began to bleed profusely from the vagina. She had been in excellent health before. She was not pregnant, and she apparently had no constitutional disease. No disorders of menstruation were present. The hemorrhage continued until after admission; it was painless and there were no subjective symptoms present, except weakness. The blood count on admission showed hemoglobin, 35; red blood cells, 1,020,000; white blood cells, 23,500; polynuclears, 91 per cent. The bleeding was controlled by packing the vagina. The next day the count showed hemoglobin, 15; red blood cells, 990,000. The patient now showed signs of marked exhaustion and weakness, the pulse was rapid and

extremely weak, and it was decided that the only hope for recovery lay in blood transfusion. The husband was summoned and 400 c.c. of blood were given to the patient, using the Kimpton-Brown tubes and the usual technic. Some difficulty was met with in getting the blood to run into the tube, as the paraffin had almost obstructed the lumen in the tip. Immediate improvement occurred. The blood count immediately after transfusion showed hemoglobin, 19, and red blood cells, 1,117,000. The leukocytes had been as high as 39,000, but dropped in direct proportion as improvement occurred. The coagulation time was eight minutes. This patient is still in the hospital and improving very slowly. The blood counts are practically alike, the hemoglobin per cent. varying from 19 to 21 and the red cells from 1,000,000 to 2,000,000. However, the general condition is better and no further bleeding has occurred. The diagnosis must of necessity be vague. Essential uterine hemorrhage most probably is the correct diagnosis. We are endeavoring to get a brother of the patient and repeat the transfusion at an early date.

CASE IV.—F. B., male, aged twenty-two years. Admitted September 11, 1915, from the Medical Wards, where he had been suffering from an arthritis of the knee. A rapidly progressing anemia and the occurrence of a suppurative condition of the joint caused him to be sent to surgical side of hospital. His hemoglobin was 73 on admission to the medical ward, the leukocytes were 25,700, with 94 per cent. polynuclears. On admission to the surgical ward the hemoglobin was 52 and the red cells 3,100,000. The knee-joint was opened and drained, but no improvement was noticed. The blood count two weeks later showed hemoglobin, 31, and red blood cells, 1,920,000. The man was desperately sick and it was decided to try blood transfusion. A brother consented to give blood, and 500 c.c. were introduced in the vein of the patient. Only a slight improvement was noted, and the next day the patient was removed to his home by request of the family. He died a few hours after arriving home. No trouble was encountered with the technic in transfusing. The Kimpton-Brown tubes were used. The donor showed no bad results, immediate or remote. It is proper to emphasize here the uselessness of trying blood transfusion when the recipient has a septic condition present, such as this patient showed. Suppuration, fever, chills, combined with a rapidly progressive anemia, constitute a contra-indication for blood transfusion. Moreover, there is an element of danger to the donor present in cases of general sepsis.

CASE V.—D. H., female, aged thirty-eight years. Admitted with a history which led the surgeon to operate at once for ruptured ectopic gestation. The rupture had evidently occurred two days previously. She had been treated on the assumption that she had some other trouble. Just before operation the blood count showed

hemoglobin, 53; red blood cells, 2,880,000; white blood cells 20,100, with 87 per cent. polynuclears. Under ether anesthesia the abdomen was opened and a tubal rupture at the fimbriated extremity was found. The belly cavity contained an enormous quantity of blood. The following day the hemoglobin had dropped to 36 and the red cells to 2,050,000. At this time she began to show signs of a general peritonitis. She was distended, peristalsis was absent and stomach lavage showed typical peritonitis vomitus. The blood count showed a rapid diminution in red cells and hemoglobin. Blood transfusion was resorted to two days after operation, the husband being the donor; 400 c.c. of blood were given and a marked improvement resulted for a day. Death occurred, however, in another twenty-four hours, due to a pulmonary edema and a general peritonitis. There was, unfortunately, no blood count taken after the transfusion. The patient in this instance was a poor risk in every way. She was extremely obese and her heart showed a moderate degree of myocardial insufficiency. We feel that it is futile to attempt transfusion when such an overwhelming infection as peritonitis is present. It is reasonable to assume that recovery would have followed had the above complication not occurred. No difficulty was met with in doing the transfusion other than keeping the large corks in the tubes.

CASE VI.—A. E., female, aged forty-four years. Admitted July 17, 1915, with a history of gall-stone disease of eighteen years' duration. The gall-bladder at operation was found full of stones, and there was a large carcinomatous mass at the head of the pancreas. A cholecystostomy was done and the subhepatic fossa drained with a rubber tube. Immediately after operation the wound began to ooze around the drainage. She was given 3250 c.c. of normal salt solution, intravenously, with a marked improvement. The oozing, however, persisted and five hours after operation, she was given 750 c.c. of human blood, which was taken from her oldest son. The dressing was changed to ascertain the amount of subsequent bleeding. There was absolutely no further staining of the dressing sixteen hours after the transfusion when the patient died.

The blood count on admission was: hemoglobin, 80; red blood cells, 4,180,000; white blood cells, 15,950; polynuclears, 80 per cent. The blood count four hours after the onset of the hemorrhage showed absolutely no change in the percentage of hemoglobin and red blood cells. This we have noted so frequently in cases of acute hemorrhage, but after ten to twelve hours, when the circulation has established itself, the change is very perceptible.

CASE VII.—F. R., female, aged forty-eight years. Admitted August 22, 1915, with a history of gall-stone disease of twenty years' standing. She was operated August 26, 1915. At operation the gall-bladder was found anastomosed to the duodenum, with a stone entirely occluding the ampula of Vater. The natural chole-

cystoduodenostomy was released and the opening in the duodenum was repaired. A markedly diseased gall-bladder, containing many small stones, was removed; the common duct was drained and the appendix was removed. The patient did very well until September 13, 1915, when she had two large stools, containing quantities of dark blood. She vomited four times, and in each of these vomiting spells the blood was bright in color and large in amount. These two bowel movements and four attacks of hematemesis occurred in a period of two and a half hours. She was given 20 c.c. of horse serum subcutaneously, but six hours after the onset of the hematemesis was still vomiting small quantities of bright red blood. She was given 400 c.c. of blood from her oldest son by the Kimpton-Brown method. After this she improved some, but still vomited small quantities of bright blood. Three days after the first transfusion she was given 750 c.c. of blood from her second son. Improvement was marked before the completion of the transfusion. She had no further hemorrhages, and the patient left the hospital in good condition, after a stay of three weeks, following the second transfusion. On admission the blood count showed hemoglobin, 69; red blood cells, 3,930,000; white blood cells, 4600; polynuclears, 58. On September 13, 1915, following the first attack of hematemesis and melena, her hemoglobin was 51 and red blood cells, 2,360,000. After her first transfusion she showed 49 per cent. hemoglobin and 3,420,000 red blood cells. After the second transfusion her blood showed 63 per cent. hemoglobin and 3,430,000 red blood cells.

CASE VIII.—P. B., male, aged twenty years. Admitted November 25, 1915, with all the symptoms of duodenal ulcer of one year's duration. Was operated November 29, 1915, when a duodenal ulcer of the first and second portion of the duodenum was found. A pylorectomy, posterior gastro-enterostomy, and appendectomy were done. The next morning the patient showed all the signs of internal hemorrhage. He was opened, a gastrotomy was done and bleeding, which was very slight, found on the posterior margin of the gastro-enterostomy. The entire gastro-enterostomy was sewed with chromic gut. The patient was put back to bed, but continued to vomit bright red blood. The night of the second operation he was transfused with 800 c.c. of human blood, which was taken from a friend. His condition improved immediately. He has not vomited since the morning after the transfusion, and at that time the blood was "coffee ground" in type. The patient remained in the hospital some time and was in good condition. His blood count on admission was: hemoglobin, 74; red blood cells, 4,790,000; white blood cells, 6900; polynuclears, 55 per cent. The morning after the first operation the hemoglobin was 67 and the red blood cells, 4,060,000. The afternoon after the second operation, hemoglobin was 68; red blood cells, 4,240,000.

Here again we see that there is only slight diminution of the

hemoglobin and erythrocytes in acute hemorrhage. A week before discharge he showed hemoglobin 46; red blood cells, 2,550,000.

CASE IX.—S. A., female, aged thirty-eight years. Admitted August 23, 1915, with a history of ruptured extra-uterine pregnancy of three and a half day's duration. She was operated upon and a rupture of the right tube found close to the uterus. The tube was removed. She was transfused with 3500 c.c. of normal salt solution on the table. She was so weak and anemic that we feared a fatal outcome. She was given 800 c.c. of human blood taken from her oldest son. She improved from a semicomatose condition to complete consciousness; her color improved and her pulse was full, slow, and of good volume. On admission her blood count showed: hemoglobin, 30; red blood cells, 1,580,000; white blood cells, 5300; polynuclears, 73 per cent. After operation and the normal salt solution transfusion she showed hemoglobin, 23; red blood cells, 1,490,000; after the transfusion with human blood, hemoglobin, 35; red blood cells, 2,070,000. A week later she showed hemoglobin, 48; red blood cells, 3,030,000. She left the hospital at the end of seventeen days in good condition, perfectly able to get around and do things for herself. Her hemoglobin was 58; red blood cells, 3,600,000 upon discharge.

CONCLUSION. While our experience with blood transfusion has been limited to 9 cases, we have been greatly impressed by the value and extreme simplicity of the Kimpton-Brown method of blood transfusion.

No patient suffering from grave anemia, particularly due to hemorrhage, should be denied the chance of recovery offered by blood transfusion.

The technic of blood transfusion by the methods of Kimpton-Brown, Lewisohn and others is so simple that everyone doing active surgery should be prepared at all times to resort to one of the several above methods.

No harm follows blood transfusion in any case, but there should be a proper selection of suitable cases. It is futile to try transfusion on cases of infection such as were encountered in 3 of the cases reported in this article.

Some little experience is needed before one can effectively coat with paraffin the tubes used by Kimpton-Brown.

The use of corks in the tubes may be an annoying and disturbing factor, but using the palm of the hand instead of a cork does away with this element of trouble.

It is a mistake to have the donor and recipient placed close to one another. Put them at opposite ends of the room, or even in separate rooms, thereby decreasing their anxiety and adding to the comfort of the operator. Too many assistants make for trouble. Our experience taught us to have ample room, the proper instruments, several extra tubes at hand, and enough melted paraffin to coat them if needed.

## TIME RELATIONS OF GASTRIC PAINS, WITH SPECIAL REFERENCE TO GASTRIC ADHESIONS.<sup>1</sup>

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IN the following paper I shall limit myself to a discussion of the pains produced by hyperacidity, perigastritis, and gastroptosis, and only incidentally to a few closely related causes.

The present status of the site of production and the method of transmission of sensation from the gastro-intestinal tract is very unsatisfactory. Lemander,<sup>2</sup> working with patients laparotomized under local anesthesia, concluded that the abdominal viscera were completely insensitive to painful stimuli and that all such sensations arose from the parietal peritoneum and subserous tissues supplied by cerebrospinal branches. Kast and Meltzer,<sup>3</sup> working with animals came to directly opposite conclusions, namely, that the viscera themselves and the visceral peritoneum were extremely sensitive under normal conditions. Third, we have the theory of Hertz<sup>4</sup> that while the ordinary methods of producing pain, such as pinching, cutting, burning, etc., do not give rise to painful sensations in the hollow viscera, yet there is one form of stimulus which he calls the adequate or specific stimulus, in this case distention, which can do so. This he demonstrated by introducing a rubber balloon attached to a manometer into the esophagus and stomach. In the former a pressure of about 50 mm. of mercury and in the latter about 15 mm. pressure produced a sensation of fulness. Distention beyond this produced a sensation of pain. Such a rise in pressure would be produced by violent contractions in the pyloric portion of the stomach or in intestinal colic. All in all the weight of evidence seems to be in favor of the lack of sensibility of the mucosa and submucosa, the sensitiveness of the muscular layer to rises in pressure, and the pronounced sensibility of the parietal peritoneum and possibly of the visceral peritoneum. The localization of pain sense in the viscera is poor, owing possibly to the paucity of nerve fibers.

Clinically, the lack of sensibility of the mucosa is evident from the painlessness of acute ulcerations anywhere in the intestinal tract, as in typhoid fever, and of superficial tubercular ulcers. The following case illustrates the same in gastric ulcer:

M. W., aged thirty years, entered the hospital for hematemesis beginning twenty-four hours previously. He had no pain or

<sup>1</sup> Read before the South Side Branch of the Chicago Medical Society.

<sup>2</sup> *Leibschmerzen; ein versuch einige von ihnen zu erklären*, Mittheil. a. d. Grenzgebieten, 1906, xvi, Heft 1.

<sup>3</sup> *Die Sensibilität der Bauchorgane*, Mittheil. a. d. Grenzgebieten, 1909, xix, 586.

<sup>4</sup> *The Sensibility of the Alimentary Canal*, London, 1911.

abdominal distress of any kind before that time. Operated by Dr. Andrews. Serosa of stomach normal. Wall incised and acute superficial bleeding ulcer found on anterior wall, near the lesser curvature.

Painful muscular contractions occur most frequently at the pyloric end of the stomach, and are due to an exaggeration of the normal reflex. The mechanism for closing the pylorus being apparently the presence of acid in the duodenum, one might think that an excessive amount of acid would inevitably result in a painful spasm. Such is not the case, however, for the introduction of a 0.5 per cent. hydrochloric acid into the normal stomach causes no sensation, while the same amount introduced into stomachs with ulcer often but not invariably causes pain.

The fact seems to be that the deepest layers of the stomach walls, especially the muscular, contain more afferent nerve fibers than the mucosa; hence the ulcerated areas, when irritated, cause an exaggeration of the pyloric reflex, often with normal and still more so with hyperacid secretion. The same fact is indicated by the incisura or local muscular spasm seen fluoroscopically on the greater curvature opposite an ulcer on the lesser. Since partial contractions of this sort do not raise the intragastric pressure they are painless. According to Hertz's theory the sensation produced by pylorospasm varies from a feeling of fulness to the typical hyperacidity pain, relieved by milk, alkalies, etc. The time of occurrence is about the time of greatest acidity, from one to three hours after eating, *i. e.*, the so-called late pains, often varying according to the quantity and quality of food taken. If gastric secretion continues between meals, *i. e.*, if it assumes the type of a continuous secretion, as often happens where motility is markedly impaired, the same pain, due to the same cause, is apt to occur at any time during the night, and to be relieved by the vomiting of varying amounts of gastric juice. This combination of late pains and night pains is the classic syndrome of ulcer of the duodenum, but this conception should be broadened to include ulcer anywhere in the stomach. The following is an illustration:

J. B., male, aged twenty-five years, entered the hospital complaining of severe continuous pain and signs of a general peritonitis. For one and a half years previous he had pain two or three hours after eating, and sometimes at midnight, which would be relieved by soda. Operation by Dr. Greensfelder. Perforated ulcer on the anterior surface of the stomach, two and a half inches from the pylorus.

L. W., male, aged forty-nine years. For thirteen years had pain in the epigastrium, coming on about one hour after meals, gnawing, cramp-like, which would be relieved by further eating. Sometimes awakened at night by pain. Gastric analysis showed normal acidity, but slightly impaired motility. Operation (Dr. Greensfelder) disclosed a callous ulcer of the lower curvature well toward



the cardiac end. An irritation then toward the cardiac end is capable of reflexly producing the duodenal syndrome, and that without any hyperacidity being present.

The impaired motility in these cases is due to pylorospasm and not to any organic obstruction.

The exaggeration of the pyloric reflex, which is the basis of the late pains, is most frequently associated with hyperacidity, with or without ulcer. In the so-called vagatonic individuals we not infrequently have the combination of visceroptosis, hyperacidity, and late pain without ulcer.

The following is taken from a report by Schmieden and Ehrmann<sup>5</sup> on forty operated stomach cases:

Mrs. M. F., aged thirty-two years. For eight years had hunger pains, *i. e.*, late pains and night pains, with free intervals. Pains radiate to back. Stomach contents: total acidity, 90. No blood. Operation: nothing found except gastropotosis.

The duodenal syndrome in patients with visceroptosis is not at all rare. Cole, of New York, has demonstrated radiographically pylorospasm due to reflexes from the terminal ileum and cecal region. The same thing may happen from reflexes arising elsewhere in the body, as in the following:

Mrs. M. B., aged forty-one years. For three years she had attacks of pain three or four hours after meals, and frequently during the night. Relieved by drinking water. She does not vomit, but has a choking sensation and becomes dyspneic. At present she has an attack about once a month. Has lost fifteen pounds, and feels very weak. Physical findings: fibroid phthisis of both upper lobes. Roentgen-rays (Dr. Turley) showed marked spasm of pylorus and retraction of right diaphragm, besides verifying the lung findings. Stomach contents: normal acidity and motility. No blood in stomach contents or stool. With rest and diet, pains improved rapidly. The reflex here might be by way of the pulmonary branches of the vagus, just as the hyperacidity which is sometimes found in incipient pulmonary disease is supposed to be.

The night pains are sometimes associated with marked pyloric obstruction, as scirrhus with much retention, when there is apt to be a feeling of fulness all day long, but pain and vomiting only at night. Evidently the peristalsis becomes excessive only then.

The class of pains, however, to which I wish particularly to call attention consists of the intermediate ones coming on about fifteen minutes to one hour after eating. The average is twenty to thirty minutes after a meal. The sensations vary from a feeling of fulness to a sharp pain, with vomiting, lacking the boring or gnawing character of the typical late pains, and are not relieved by more food or alkalis. They are sometimes quite well localized, and their point of origin is sensitive on pressure. The usual explanation is

<sup>5</sup> Magendiagnostik, Mittheil. a. d. Grenzgebieten, 1914, xxviii, 359.

that they are the same as the late pains, only the pylorus has become edematous or only more irritable, so that the spasm appears earlier. In some cases this is true, but I believe that more often they are the result of adhesions between the stomach and neighboring organs. It is to be remembered, of course, that the most extensive adhesions may exist without symptoms, especially if between two movable organs, as coils of small intestines. Those most apt to cause disturbances are the broad, thick bands fixing the pylorus and the lesser curvature to the peritoneum of the liver or the posterior abdominal wall. The cause of the pain in the majority of cases is, I believe, mechanical, being due simply to a pull on the nerves of the sensitive subperitoneal tissue. They begin, as a rule, when gastric peristalsis begins to reach its height, namely, fifteen to twenty minutes after a full meal. The time of occurrence is independent of the situation of the adhesions.

M. F., aged forty-two years. For two years had cramp-like pains in epigastrium, beginning shortly after eating and lasting two or three hours. No nausea or vomiting but marked eructations. Operation by Dr. McArthur. Ulcer of pylorus, with marked adhesions to the duodenum.

On the following case of Dr. Hamburger.

Miss B., aged twenty-eight years, had a gastric hemorrhage fourteen years ago. For the last six years she has had pain one-half hour after eating, lasting two or three hours. Stomach contents showed diminished acidity and normal motility. Operation by Dr. Greensfelder. Adhesions between the greater curvature and the anterior abdominal wall and from the lesser curvature and the pylorus to the gall-bladder region.

C. M., aged twenty-eight years. Operated on six years ago for appendicitis. Now complains of pain with nausea fifteen minutes after eating. Examination shows enlarged spleen; stomach contents normal. All other findings normal. Operation showed thick adhesions between the stomach and spleen, the etiology of which the operation did not disclose.

Included in this group of traction pains are those familiar ones of epigastric hernias. They all have the characteristics cited above, and are generally conceded to be due to pull on the omentum. An interesting group is formed by those cases in which we have combinations of early and late pains. For instance:

A. T., aged thirty-eight years. Operated on in St. Louis two years ago for ulcer of the stomach. Now has sharp pains, at times, twenty to thirty minutes after meals, and sometimes two to two and a half hours after meals. Stomach contents: moderate hyperacidity and impaired motility. Roentgen-rays (Dr. Turley) and later operation (Dr. Andrews) showed the old gastro-enterostomy opening patent and a broad band of adhesions between the antrum and the liver. Interpretation: late pain due to hyperacidity, early pains due to adhesions.

Another case illustrating the transformation of one type of pain into the other is the following:

I. F., aged thirty years. One year ago had severe pains with nausea and occasional vomiting, one to one and a half hours after eating. Pain relieved by eating. Improved for a while after treatment. Now has a burning pain in the epigastrium ten to fifteen minutes after eating, not relieved by more food. Stomach contents: marked hyperacidity and impaired motility. Evidently here the ulcer had progressed until the peritoneum was involved and adhesions formed, hence the change in the time of the appearance of the pain. The operation (Dr. Andrews) disclosed a pyloric ulcer so adherent that the stomach could not be brought forward.

Another type of pain is the continuous one, generally with exacerbations after meals, and sometimes vomiting. As in the other types, it varies from a feeling of fullness through a dull ache to a sharp pain, radiating to the back. Such pains are due most frequently to one of the following causes: (1) penetrating ulcers, with marked peritoneal reaction, *i. e.*, peritoneal thickening or adhesions; (2) rapidly growing carcinoma; (3) marked gastric stasis due to organic or functional pyloric obstruction, benign or malignant. The following case is an example:

J. Z., aged forty years. Had burning in epigastrium for seven years, relieved by soda. Recently a continuous dull, gnawing pain, worse one to two hours after eating. Stomach contents showed good motility and moderate hyperacidity. The operation (Dr. Andrews) disclosed an ulcer scar at the pylorus which was so adherent that it could not be brought forward.

It seems reasonable to conclude here that when the adhesions reached a certain grade the continuous dull ache began while the late pains persisted. I cannot explain why adhesions at one time cause a continuous discomfort and why at other times adhesions just as dense in the same position cause pain only when peristalsis is at its height, but I dare say that the sensitiveness of the individual comes into play here. Another example:

A. G., aged fifty-four years, entered Dr. Edwards's service with a history of rather sharp pain for the last year, coming on one to two hours after meals. This attack lasted four months. Then for four to six weeks had epigastric distress fifteen minutes to one hour after meals, with some vomiting. Then felt better for a while. Three months ago the pains recurred, and are now almost continuous, but worse after meals. Examination: marked impaired motility. Total Acidity, 45. Operation (Dr. McArthur) showed carcinoma of pyloric end of stomach adherent to posterior abdominal wall and many metastases. The continuous pain here was not in any way different from the case mentioned above. Another example:

E. S., aged forty-nine years, entered Dr. Edwards's service. Has had pain for five years, beginning fifteen minutes after meals.

and radiating to the back. Besides this a constant dull ache. Also frequently awakened at night by pain. Nausea and vomiting frequently. Stomach contents: hyperacidity and impaired motility. At operation (Dr. McArthur) a large callous ulcer was found in the cardiac portion of the lesser curvature. No adhesions or pyloric obstruction. For the late pains we have the usual explanations. For the continuous ache we might postulate a continuous pylorospasm or possibly the marked thickening of the peritoneal covering of the ulcer might account for it, and the same for the early pains, which were also present in this case.

As one of the frequent causes of adhesions to and near the pylorus we may consider the gall-bladder separately. As a general rule it may be stated that when the gall-bladder is not pathologically connected with the stomach, *i. e.*, by adhesions, the pains are far less likely to have a constant relation to meals than otherwise. The acute gall-stone attack has no constant relation, while empyema and hydrops, or the shrunken gall-bladder adherent to the surrounding liver substance, tend to produce a constant ache, with exacerbations, independent of food-taking. It is quite common, for instance, to get a history of one or more acute gall-bladder attacks with perfectly free intervals, and finally a constant dull ache, and to find at operation a greatly distended gall-bladder. It is unnecessary to cite instances of this common occurrence. When, however, a pericholecystitis with coarse bands of adhesions to stomach or duodenum is present the usual rules hold, and we have most often an early pain, or occasionally a late pain, especially if hyperacidity is present, and sometimes a combination of both. For instance:

D. S., aged twenty-six years. For the past few months had pain and vomiting—sometimes immediately and sometimes one and a half hours after eating. No gastric analysis. Gall-bladder at operation found adherent to omentum, duodenum, etc.

Mrs. P. R., aged sixty-six years. For eight years had attacks of pain in the right hypochondrium every six to eight months. Since the last attack has had distress for fifteen to twenty minutes after meals, especially after eating meat. No nausea or vomiting. Operation by Dr. McArthur. Thickened gall-bladder with dense adhesions to stomach and duodenum.

Other less usual types of gastric adhesions may be mentioned, *e. g.*, those to the anterior abdominal walls. Here there are early pains, and others arising on exertion and relieved on lying down. The commonest examples are ventral hernias, already mentioned.

C. G., aged thirty-six years, was operated in 1908 for gall-stones. Returned the following year with pains coming on shortly after eating, and made worse by moving about. Operation by Dr. McArthur. Stomach adherent to anterior abdominal wall and transverse colon.

Adhesions to the transverse colon are apt to cause early or

late pains, with others at rather definite periods before or after defecation.

The final group of pains I shall consider consists of those occurring within the first fifteen minutes after taking food, and varying, as the other types, from a slight distress or feeling of fulness to severe gastralgia, radiating to the back, along the sternum and so forth. These may, of course, be due to obstruction of the cardia, either functional or organic, but I wish here to call attention to those due to neuroses and enteroptosis. In simple neuroses, without changes in the gastric secretion, where the pain is apparently due to hyperesthesia of the gastric mucosa, it is apt to come on immediately on taking food, no matter how small in amount. It is unnecessary to give examples of these. The distress in gastropptosis occurs also, as a rule, very shortly after eating, is often described as a burning sensation, is frequently relieved by lying down, and often increased by a bowel movement, owing possibly to a diminution in intra-abdominal pressure. An example is the following:

Mrs. R., aged forty-nine years. For several years has had a feeling of fulness fifteen to twenty minutes after eating, depending on the quantity of food more than on the kind. Less marked on lying down. Feels weak and has lost some weight. Examination: general visceroptosis and moderate hyperacidity. Roentgen-rays confirmed the former. Forced feeding and complete rest caused amelioration of symptoms. An example of late pains in gastropptosis from the accompanying hyperacidity was given above (Ehrmann and Schmieden's case<sup>6</sup>).

To sum up, then, we may divide gastric discomfort of the intra-gastric and perigastric regions into continuous and intermittent varieties. The continuous pains are most frequently due to carcinosis, to marked pyloric obstruction, and to penetrating ulcers, with peritoneal involvement. The intermittent pains may be divided into immediate, early, and late. The immediate are found frequently in ptosis, neurosis, obstruction of the cardia, besides other conditions, not considered here, as *achylia gastrica*, etc.

The early pains, including those occurring fifteen to sixty minutes after eating, are most often due to adhesions in any part of the stomach, including ventral hernias and pericholecystitis. These are to be thought of particularly in those cases where the changes in secretion and motility are too slight to account for the distress complained of.

Late pains include those occurring one to three hours after eating, and indicate an increase in intragastric pressure or pylorospasm, of which the most frequent cause is hyperacidity. It is occasionally due to slight pyloric obstruction or pyloric adhesions or reflex causes.

<sup>6</sup> Loc. cit.

## REVIEWS

AUTOPLASTIC BONE SURGERY. By CHARLES DAVISON, M.D., Professor of Surgery and Clinical Surgery, University of Illinois, College of Medicine; Fellow of the American College of Surgeons; Surgeon to Cook County Hospital and University Hospital; and FRANKLIN D. SMITH, M.D., Clinical Pathologist to University Hospital. Pp. 369; 174 illustrations. Philadelphia and New York: Lea & Febiger, 1916.

This book is an important contribution to clinical surgery. It is seriously marred, however, by the method of presentation of the valuable pathological matter contained in the first three chapters.

The book would not suffer if these three chapters were entirely omitted, inasmuch as the clinical part of the work exemplifies the pathological teaching with sufficient emphasis. This teaching, which seems supported by the experimental work, is briefly as follows, insofar as its practical applications to surgery are concerned: the cambium layer of the periosteum, or the periosseous osteogenetic layer, as it is here called, cannot readily be separated from the bone cortex; and it is impossible to tell from macroscopic inspection, after separation of the periosteum, whether or not any of this cambium layer has been removed with the periosteum. What is more, it is necessary to examine the denuded cortex microscopically to be sure that none of the cambium layer has been left attached to it. The conclusion is that the periosteum as a readily separable membrane has little or no osteogenetic properties, being merely, as Macewen contended, a limiting and protecting membrane; and that it should be left attached to the transplant only when the latter is to be exposed among soft tissues, but is actually detrimental to the transplant when this is embedded in bone. This conclusion pleases the reviewer, as it has been his contention that the periosteum merely serves to prevent an exposed transplant from disintegration by the surrounding tissue cells; and because it has been his practice never to leave the periosteum attached to the transplant when the latter was to be completely buried in osseous tissue. Furthermore, the authors of this book think the endosteum and marrow are negligible factors in bone transplantation and repair, claiming paramount importance for the cortical bone, which from the very fact of its denseness and its poverty of circulation, is fitter to withstand transplantation and to preserve its vitality by nourishment from its own contained fluids and by osmosis from surround-

ing structures, than are the more highly specialized elements in the transplant on which other clinicians have placed most reliance.

Now from these pathological foundations, Dr. Davison has erected his technical application of bone transplantation in surgery. Chapter IV describes the indications for autoplasmic bone surgery and Chapter V the instruments employed, which are comparatively few in number and simple in design. Chapter VI, of 100 pages, is devoted to descriptions of bone transplantation as applied to recent fractures, and Chapter VII (52 pages) to the treatment by similar means of ununited fractures. The remaining chapters (VIII to XI) describe tersely, but with sufficient detail, the applications of autoplasmic bone surgery to tuberculous spondylitis, and to congenital and acquired deformities, such as spina bifida, cranial defects, defects following excision of the diaphyses or epiphyses of long bones, nasal deformities, etc. An interesting suggestion is that by Dr. Smith for enlarging the female pelvis by implanting bone in the symphysis pubis.

Dr. Davison's experience appears to have been confined mainly to fracture work, of which some twenty-five cases are quoted at considerable length. The skiagraphic results are indeed marvelous, and surpass anything published elsewhere by any method of fixation; but it would be of more interest to ascertain in greater detail the functional result and the duration of the patient's absence from work. It is to be hoped that a complete statement of such matters will be submitted to the Committee on Fractures of the American Surgical Association for inclusion in their next report.

For immobilization he employs a medullary peg in preference to an inlay transplant, and prefers to use a section of the fibula (removed subperiosteally) for this purpose whenever the interior of the fractured bone is large enough to receive it. He lays much stress on the value of fitting such an irregularly shaped peg into a round hole, and when using transplants cut from the tibia for medullary pegs or for pegging the cancellous ends of the long bones, he cuts these pegs three- or four-sided and drives them into a round hole, thus preventing rotation of one fragment on the other much more certainly than when a cylindrical peg is used, as practised by Albee. The inlay transplant he thinks of little use except in the middle of the shaft, and rarely employs it except in ununited fractures of the tibia with the fibula united, where fracture of the fibula would be necessary to insert an intramedullary peg into the tibia.

The author presents his case reports without comment, and throughout the volume gives cheerful recognition to other workers in the same field, and is withal commendably modest in regard to his own very evident technical skill. The best book we know in any language on the purely operative treatment of fractures from a mechanical point of view, is that by Lambotte; the present

volume reminds us constantly of that work in its close attention to mechanical details and its systematic exposition of operative technic. It is not too much to say that in these respects it contains the best account in English of the treatment of fractures by autoplasmic bone surgery.

A. P. C. A.

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PRINCIPLES AND PRACTICE OF OBSTETRICS. By JOSEPH B. DE LEE, A.M., M.D., Professor of Obstetrics at the Northwestern University Medical School. Second edition, thoroughly revised. Pp. 1087; 938 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE fact that a second edition of this book was demanded in so short a time is ample proof of its popularity. It has evidently been thoroughly revised and is up to date in practically all particulars. Especially valuable to the student and teacher are the chapters on mechanism of labor and deformities of the pelvis, of all subjects in obstetrics probably the most difficult to explain satisfactorily to a student. The illustrations showing the "touch picture" in different presentations should prove of great value. Two subjects merit more than the scanty notice they receive, cystoscopy and pyelitis. Another section which will not meet with wide approval is that on perineal lacerations and their repair. The descriptions of the injuries suffered do not coincide with the more modern findings.

BUT there is so much that is excellent in the book and so little that can with fairness be criticized on any other grounds than a justifiable difference of opinion, that the book must be regarded as a most valuable contribution to our libraries.

J. C. H.

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KEEPING PHYSICALLY FIT. By WM. J. CROMIE, Instructor in Physical Education, University of Pennsylvania; Director of the Summer School Courses in Physical Education, University of Pennsylvania, etc. Pp. 146; 41 illustrations. New York: Macmillan Company, 1916.

THIS work is written by a man peculiarly fitted for handling his subject. For sixteen or more years he has been actively engaged in teaching exercise to men, women, youths, and children. He here sums up what he has found, throughout these years of careful observation to be the best for pupils physically and mentally. He lays great stress on the co-relation of mental and physical



activity, and the influence of eating, drinking, bathing, rest, sleep, fatigue upon health. He discusses exercises for the busy man, for the nervous woman and for the growing child; appropriate exercises for each class are described and illustrated. No great length of time, no special apparatus is needed, a few moments each morning practising natural muscular movements, he claims, will keep the body fit and consequently greatly increasing the capacity for brain work.

The work is well expressed and presents his points forcibly, making very pleasant and instructive reading. E. L. E.

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DIAGNOSTIC AND THERAPEUTIC TECHNIC. BY ALBERT S. MORROW, A.B., M.D., Clinical Professor of Surgery in New York Polyclinic; Attending Physician to Workhouse Hospital and Central and Neurological Hospitals. Pp. 834; 860 illustrations. Second edition. Philadelphia and London: W. B. Saunders Company.

IN the preparations of this the second edition of *Diagnostic and Therapeutic Technic*, the manuscript has undergone an extensive revision and much new material has been added. This amplification includes the addition of many new illustrations and the redrawing of many of the old.

The present edition fills more perfectly than even its most successful predecessor did, the niche in medical literature for which it was originally designed. It makes possible, without any extended reading or reference a knowledge of just how to correctly perform the more usual and many of the less common procedures of a mechanical nature with which every practitioner is periodically brought face to face. The large and clear illustrations are as valuable as the text. To one who is not constantly called upon to perform these semi-surgical procedures the book stands in the place of a friend whose advice and caution may at a moment's notice be sought. As the memory of detail is so easily dulled by time it is a comfort to have such a friend always at hand.

Indeed, to no one friend could one turn to obtain all the pertinent information regarding local and general anesthesia, intravenous infusion, venesection, hypodermic and intramuscular medication, exploratory puncture and aspirations, and the mechanical procedures referable to the stomach.

While, to be sure, much of the book is devoted to so-called special work, it is surprising how many of the maneuvers relative to the eye, ear, nose, throat, larynx, trachea, esophagus, colon, rectum, urethra, bladder, ureter, kidneys and female generative organs will fall within one's grasp if the opportunity here offered to master them is taken.

The section devoted to abdominal examination is especially concise and good. For the more hardy practitioners who care to tread the ground, transfusion of blood, injections for neuralgia, and other decidedly special procedures are outlined.

As a saver of time and a multiplier of efficiency this book can hardly be spared from any bookshelf. A. A. H.

**GAS-POISONING IN MINING AND OTHER INDUSTRIES.** By JOHN GLAISTER, M.D. (Glas.), D.P.H. (Camb.), F.R.S.E., Professor of Forensic Medicine and Public Health in the University of Glasgow; Senior Medico-Legal Examiner in Crown Cases for Glasgow and Lanarkshire, etc., and DAVID DALE LOGAN, M.D., (Glas.), D.P.H., Surgeon to the Coltness Ironworks, Newmains, etc. Pp. 471; plans, colored plates, and 36 other illustrations. New York: William Wood & Co.

IN these days when our interest is so centered on war, and when the hideous agencies employed for destruction are familiar to us all, it is only natural that we should be misled by the title "gas-poisoning" on the cover of this book. But far from being a discussion of the poison gases used by man to destroy his fellow the work is concerned with those poisonous gases which endanger the health or life of the great army of industrial workers. And the story of the battle waged underground in coal mines against the combined forces of choke-damp, fire-damp, stink-damp, and after-damp make as fascinating reading as the account of any martial exploit.

The book is chiefly concerned with carbon monoxide, which is the most important of the industrial poison gases, and which is accidentally produced in a most amazing variety of ways. Miners are, of course, most exposed, but many cases are cited where poisoning occurred in very unexpected manners. The possible methods of production of carbon monoxide and other gases are fully considered in the first five chapters, and then follows a very careful description of the symptoms of gassing by these poisons. By many readers the great variety of disorders which can be produced by such poisoning will have been unsuspected. The pathology of carbonoxide poisoning is thoroughly reviewed, and chapters are devoted to the treatment of the patient, the methods of detecting carbon-monoxide gas in the blood and in the air and to the apparatus for rescue and aid work in mines.

The book is well written, carefully edited, and an extensive bibliography is appended. It will be of interest to all members of the medical profession as well as to all who are concerned with industries in which gas is employed. To these latter it will appeal especially because of the recent adoption of workmen's compensation legislation.

O. H. P. P.

DISEASES OF CHILDREN. By HENRY DWIGHT CHAPIN, A.M., M.D., Professor of Diseases of Children in the New York Post-Graduate Medical School and Hospital, and GODFREY ROGER PISEK, M.D., Sc.D., Professor of Diseases of Children and Attending Physician to the New York Post-Graduate Medical School and Hospital. Third revised edition; pp. 578; 179 illustrations; 12 colored plates. New York: William Wood & Co., 1915.

THE authors, possessed of a wide experience in teaching pediatrics, have presented the subject in clear, concise, and practical terms. It is at once a text-book for the student and a safe guide to the physician.

The importance of clinical findings at the bedside have been emphasized and the student familiarized with methods to be employed in making a systematic examination of the patient and reading a scientific diagnosis. To this end the more important and recent laboratory and clinical tests have been described, including the Schick and the luetin tests.

For teaching purposes, treatment has been presented simply and rationally. Infant feeding has been brought up to date by the authors who have largely rewritten this section, and have added newer methods, such as albumen-milk feeding.

The addition of descriptions of certain mental tests especially adapted for the early months of life add much to the value of the book, and show an appreciation of the widespread interest in prophylactic pediatrics.

J. F. S.

DER TUBERKULOSE-FORTBILDUNGSKURS DES ALLGEMEINEN KRANKENHAUSES HAMBURG-EPPENDORF. Edited by DR. LUDOLPH BRAUER, Medical Director. Vol. II. Pp. 159; 6 illustrations; 13 plates. Würzburg: Curt Kabitsch

THIS collection of articles by physicians formerly and at present connected with the Eppendorf Hospital has been published in celebration of the twenty-fifth anniversary of the institute. Like all similar collections, there are not a few articles which are of interest only to men working in special lines. The first article by Lorey upon the value of roentgen-ray examinations in pulmonary tuberculosis covers the subject in a very thorough manner. Like most of the articles of this kind, considerable stress is laid upon the value of this method in detecting tuberculosis of the tracheobronchial lymph glands and hilus tuberculosis. Brauer gives a very complete consideration of the surgical treatment of pulmonary tuberculosis with the various indications for its use, technic of the different measures employed, and the results of this form of treatment. Naturally the article deals chiefly with artificial pneumothorax

from various stand-points. Kümmell's contribution upon tuberculosis of the kidney is well illustrated by numerous colored plates and one roentgen-ray engraving. The photographs of roentgen-ray negatives for Lorey's article are beautifully sharp and clear for such reduced photographs. The colored plates of microscopic sections of compressed lung in Brauer's article also bring out the development of fibrous tissue around the tubercles in an interesting manner. Other subjects considered are tuberculosis of the eye; effect of climate, tropical and seashore, upon tuberculosis; the use of tuberculin in the treatment of this disease.

The volume forms a collection of exhaustive articles on varied aspects of tuberculosis which should prove of value as a work of reference.

F. A. C.

CHANGES IN THE FOOD SUPPLY AND THEIR RELATION TO NUTRITION. By LAFAYETTE B. MENDEL, M.D., Professor of Physiological Chemistry in the Sheffield Scientific School of Yale University. Pp. 61. New Haven: Yale University Press, 1916.

THIS small essay, presented at the Second Pan-American Scientific Congress, at Washington, deals with the question of the supply of food energy and its availability where needed, largely from the point of view of a physiological chemist. This conception of such an important economic problem is a new one and one which merits closer thought than usually given to it. The author discusses his subject in a most presentable manner. In dealing with the subject of food energy Dr. Mendel utters thoughts which are fit fodder for mental nourishment.

J. H. M., JR.

DISEASES OF THE SKIN AND THE ERUPTIVE FEVERS. By JAY FRANK SCHAMBERG, M.D., Professor of Dermatology and Infectious Eruptive Diseases in the Philadelphia Polyclinic and College for Graduates in Medicine. Third edition. Pp. 585; 248 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

IT is a pleasure to review the excellent book of Dr. Schamberg's and to congratulate the author upon the excellence of the illustrations and the clearness of the text. Comparatively few changes have been made since the last edition. The term *prurigo nodularis* has been substituted for "multiple cutaneous tumors associated with itching." Angioneurotic edema has wisely been placed after

urticaria rather than following urticaria pigmentosa. The following statement is made under psoriasis: "Schamberg, Ringer, Raiziss, and Kolmer have demonstrated by careful clinical and laboratory investigations that a high nitrogen diet aggravates psoriasis and, conversely, that a low nitrogen diet (containing about five grams daily) has a distinctly favorable influence and may of itself lead to a virtual disappearance of the eruption." While these gentlemen are to be congratulated upon their painstaking investigations the findings have yet to be confirmed by other investigators.

The luetin test has been added and a photograph is presented exhibiting the reaction. Two new conditions are described under the acute eruptive fever section: mild typhus fever (Brill's disease) and Rocky Mountain spotted fever, including a photograph of the eruption in the latter. New photographs have been added under the following diseases: psoriasis (two pictures), xanthelasma, chancre of the finger, nodular leprosy, epithelioma, sarcoma, and two illustrations of granuloma fungoides and of feigned eruptions. Cholesterinized antigen is mentioned under the Wassermann test. Zinc chloride paste is advocated as a treatment for the tumors of granuloma fungoides. The following rare, or at least infrequent, skin eruptions are not mentioned in the present volume: eczematoid ringworm, diphtheria or pseudodiphtheria of the skin, leukemia or pseudoleukemia cutis, xanthoma pseudoelastium, and paraffinoma. The metric system has been added. The present volume contains twelve more pages than the former edition. F. C. K.

PRAKTIKUM DER CHIRURGIE. EIN LEITFADEN FÜR AERZTE, CHIRURGISCHE ASSISTENTEN UND MEDIZINALPRAKTIKANTEN. By DR. O. NORDMANN, Chief of the Second Surgical Division of the Auguste Viktoria-Krankenhaus at Berlin-Schöneberg. Second Part: Special Surgery. Pp. 413; 140 illustrations. Berlin and Vienna: Urban and Schwarzenberg, 1915.

THIS is the second part of a *Hand-book of Surgery* intended for the use of family physicians and embryo surgeons. It deals only with regional surgery, and includes the minimum amount of pathology, very little in the way of diagnosis or symptoms, and only a modicum of treatment. Emergency operations are described in somewhat tedious detail; for example, trephining, tracheotomy, drainage of thoracic empyema, and appendectomy. It may be desirable for the family physician to practise such operations in emergencies, though it is doubtful whether in most instances the precarious state of the patient would not be increased by such an undertaking; and it is certain that in cases of real emergency (such

as obstruction of the windpipe) the patient would be dead several times over before the family doctor had time to read through the description of tracheotomy here given. What it is really desirable for the general practitioner to know, and what he could actually learn in many cases from the study of a good hand-book on surgery, is not taught him here. This is the early diagnosis of such conditions requiring the operations enumerated above, and of other conditions not even mentioned in the present hand-book—such for instance as the diagnosis of tumors of the breast, gastric lesions, and carcinoma of the external structures such as the lips, cheeks, tongue, cervix uteri, etc. In brief, this is not a book of a commendable type; though within its limitations it is as good as could be expected.

A. P. C. A.

DISEASES OF THE NOSE AND THROAT. By ALGERNON COOLIDGE, M.D., Professor of Laryngology in the Harvard Medical School. Pp. 360; illustrated. Philadelphia and London: W. B. Saunders Company, 1915.

THIS is a good, clearly written, little hand-book, giving in a concise form the essential facts concerning diseases of the nose and throat, and is especially adapted for the medical student and the general practitioner. While there is lacking detail and minute description in many of the chapters, the more common ailments, such as epistaxis, tonsillar conditions, hay-fever, etc., are dwelt upon in sufficient length to make it a book of real help to the general practitioner. Further, almost all of the physiological and medical data and even the newer methods of operating are at least touched upon so that a novice in nose and throat work would glean at least a comprehensive view of the whole field. There are many suggestions as to methods of examination and the relative importance of objective findings that make us realize that the author has a knowledge of his speciality gained from large clinical experience. On the whole, the book is what we might call "safe," that is, the data furnished is in accord with established facts and generally accepted fancies. We note, however, a few exceptions: one, for instance, p. 220, where it is stated that Ludwig's angina is a term applied to "a septic invasion of the submaxillary and neighboring regions," which is just what it is not. Fortunately, there are very few such misstatements. The chapters are well arranged and the index complete. The illustrations are rather crude and mostly diagrammatic in character, but well chosen for aiding one in understanding the text.

We would recommend this book very highly, especially for the medical student.

G. B. W.

# PROGRESS OF MEDICAL SCIENCE

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## MEDICINE

UNDER THE CHARGE OF

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**The Infectiousness of the Cerebrospinal Fluid in Syphilis.**—FRUEH-WALD and ZALOZIECKI (*Berl. klin. Wchuschr.*, 1916, 53, 8) point out that the pathology of syphilis of the central nervous system has been advanced a great deal through studies on the cerebrospinal fluid. After it was discovered that the *Treponema pallidum* is the cause of syphilis, it was looked for by numerous investigators in the cerebrospinal fluid, and found particularly by microscopic methods and particularly through animal inoculations. The authors' work on this particular subject was interrupted by the onset of the war, but they had advanced far enough to secure some definite positive results, which were as follows: (a) No positive results were obtained in cases of tabes or general paresis. (b) Positive results by inoculation methods were obtained in an early secondary case with manifest central nervous system symptoms, and in two others, late cases of secondary lues in one of which the spinal fluid was entirely normal, and in the other there was a positive Wassermann reaction. The authors were unable to arrive at any rule by which one might judge the infectiousness of the cerebrospinal fluid in any stage of syphilis. An analysis of the literature on the subject to date reveals the following facts: 1. Acquired lues. (1) Without nervous manifestations: (a) primary lues up to the eighth week negative; (b) primary and secondary lues eighth to tenth week, 2 positive; (c) late secondary lues, third to twelfth month, 5 positive cases; (d) tertiary lues negative. (2) With congenital nervous symptoms: (a) early luetic meningitis, 1 positive case; (b) "neurorecidiv," 1 positive case; (c) luetic apoplexy and hemiplegia, 2 positive cases; (d) late luetic meningitis, 1 positive case; (e) tabes dorsalis, 2 positive cases; (f) paresis, 5 positive cases.

*B. Congenital lues:* (a) early cases, 2 positive cases; (b) late cases, 2 positive. It will be seen from this analysis that the greatest number of positive results occur in the late secondary stage and that a relatively large number of positive findings are obtained in the later syphilitic involvements of the central nervous system. All told, however, the causative agent is found quite infrequently. Spinal fluids containing the treponema may be entirely normal otherwise, in association with a positive or negative blood Wassermann reaction and in the complete absence of nervous manifestations.

**Open Puncture of the Pleura.**—SCHMIDT (*München. med. Wchnschr.*, 1915, lxii, 873) makes further report on open puncture of the pleural cavity, a therapeutic procedure which he advocated two years ago. He employs a trocar about 8 cm. long and 0.4 cm. in diameter. He has the patient resting on two beds, the shoulders on one and the buttocks on the other. He selects the point of maximal dullness for the puncture and the patient is so placed on the beds that this point is lowermost during the tapping. When inserting the trocar, the patient may be rotated slightly, though the trocar should not be inserted when the patient is in the erect posture. The fluid is allowed to drain directly into an open vessel. Most exudates are under positive pressure, and the fluid escapes readily. After a certain amount has been evacuated, the pressure approaches zero, and finally becomes negative, at which point air rushes into the cavity with inspiration. It is not necessary to filter the air, Schmidt says, as he has never known any harmful results to follow the procedure. By having the patient in the position described, the evacuation of the fluid is much more complete than with the usual suction apparatus in the sitting posture. When the exudate is under negative pressure the fluid is practically always encapsulated. The pneumothorax produced appears to be beneficial. The author has not had to puncture the same pleural cavity more than twice. Roentgen-rays taken after the puncture are clearer, and show more definitely whether fluid is walled off in two or more pockets, and also whether marked lung changes are present. The author has also used this method in cases where the fluid was only slightly purulent, but in most cases of empyema the usual operative treatment is indicated.

**Duodenal Regurgitation and its Influence upon the Chemistry and Function of the Normal Human Stomach.**—SPENCER, MEYER, REHFUSS and HAWK (*Amer. Jour. Physiol.*, 1916, xxxix, 459) report a study of duodenal regurgitation in the normal human stomach. They employed fractional removal of the gastric contents by means of the Rehfuß tube. The experiments were all carried out on normal individuals whose last meal was that of the previous evening. The residuum was then removed, and the material under investigation was introduced into the stomach. Samples of 5 c.c. of gastric contents were then removed for study at intervals of ten minutes. This was continued until the stomach was empty. The presence of trypsin and of bile was used in determining whether regurgitation of duodenal contents had occurred. The authors found that trypsin is almost constantly demonstrable in the fasting and digesting contents of the normal human



stomach. They found normal individuals of the high acidity type usually yielded low trypsin values, while in those of the low acidity type tryptic power was marked. The latter fact suggested to the authors the possibility of tryptic digestion occurring in part in the stomach as a compensatory action in cases of low acid and pepsin secretion. They found that the introduction of 0.5 per cent. hydrochloric acid into the stomach is followed by a rapid reduction of acidity to about 0.2 per cent. hydrochloric acid or less. The fall in acidity is accompanied by a rise in tryptic values and by the presence of bile. The author's observations of the action of hydrochloric acid and pepsin upon trypsin are not without interest. Most of their experiments were done with freshly removed samples, but they have found "trypsin present in samples having an acidity of 110 c.c.  $\frac{N}{10}$  KOH which had stood for eighteen hours at room temperature. Other tests have shown that trypsin seems but little influenced by the acid and pepsin in the gastric contents." After introduction into the stomach of 5 per cent. sodium bicarbonate solution, it was found that if a prompt secretion of gastric juice failed, the solutions were held in the stomach for sometime and acquired high tryptic values and also underwent marked color changes. The retention appeared to be for the purpose of reducing the alkalinity in order to render the fluid harmless to the duodenum. With weaker solutions of alkali the secretion of acid by the stomach and neutralization were more prompt. Furthermore, fluid escaped from the stomach into the duodenum before the contents had become acid, thus indicating that acidity of the stomach contents is unnecessary for the opening of the pylorus in man, though Cannon has shown that it is in cats. The authors incline to the view that the human pylorus is controlled from the duodenum, acid fluid keeping the pylorus closed until the fluid in the duodenum is neutralized. In the human stomach, too, the authors find that weak sodium bicarbonate solutions have a stimulating effect on gastric secretion and at the same time hastens the emptying of the stomach.

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**Notes on the Urochromogen Test in the Urine.**—PULAY (*München. med. Wchnschr.*, 1915, lxii, 1009) has made comparative tests of the diazo reaction of Ehrlich and the urochromogen test of Weiss. In 125 healthy adults and in 64 vaccinated against typhoid fever (12 freshly vaccinated) both tests were negative in all instances. Of 85 cases of typhoid fever with positive bacteriological findings each test was positive in 57 cases, and, in addition, the diazo test was weakly positive in 6 more. In 7 cases of tubercenlosis the diazo test was positive in all, the urochromogen test in 5. The diazo test was also positive in all of 6 cases of pneumonia, the urochromogen test uniformly negative.

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**The Effect of Diet on the Uric Acid Content of the Blood.**—DENIS (*Jour. Biol. Chem.*, 1915, xxiii, 147) has reported observations on the effects of diet on the concentration of uric acid in the blood, which are of interest to clinicians owing to the increased importance of uric acid determinations in the differential diagnosis of obscure arthritides. Her subjects were patients in the medical and surgical wards of the Massachusetts General Hospital. The surgical patients were normal individuals except for the surgical condition (hernia or fracture), for

which they entered the hospital. The medical patients studied were suffering from nephritis and cardiorenal disease and also from various chronic diseases not associated with renal insufficiency, or with fever. Patients with gout were not available during the course of the observations. The patients were studied during a period of purin-free diet and of diet rich in purin. The blood was all withdrawn before breakfast to obviate any possible effect of a recent meal. The results of this investigation are that in normal men no increase in the circulating uric acid is produced by ingestion of large quantities of purin, while in persons suffering from renal insufficiency a more or less marked increase in the uric acid content of the blood is produced by high purin feeding, as would be expected from the recently published findings of FOLIN and DENIS (*Arch. Int. Med.*, 1915, xvi, 33). The author, therefore, concludes that "when the determination of uric acid in the blood is undertaken as a diagnostic test the insistence on a preliminary period during which no purin containing foods are consumed is unnecessary except in the cases in which kidney insufficiency exists or perhaps in persons who habitually consume extremely large quantities of purin containing foods."

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**The Diagnosis of Intestinal Perforation with the Aid of Roentgen Rays.**—POPPWE (*Deutsch. med. Wchnschr.*, August 26, 1915) calls attention to the possible use of Roentgen rays in the early diagnosis of gastric or intestinal perforation by the recognition of a clear crescent-shaped area between the dome of the liver and the diaphragm due to the accumulation of a small amount of free gas. This sign was first observed in a case of gastric ulcer with suspected perforation. Roentgen-ray examination showed this clear, crescentic area, but these findings were at first not properly interpreted. Later the patient developed a typical subdiaphragmatic abscess which was successfully drained. About a year later the patient died of carcinoma of the stomach. Subsequent studies of the Roentgen-ray plates showed that the clear, crescent-shaped area over the dome of the liver was due to the accumulation of a small amount of free gas and could be differentiated from the clear zone due to a misplaced and distended colon by: (a) The clear zone was crescent-shaped with its widest portion over the dome of the liver and becoming obliterated on both sides. (b) It is visible only when the patient is in the upright position since in the recumbent posture the gas accumulates between the surface of the liver and the anterior wall, and is therefore no longer visible in the Roentgen-ray plates. The possible importance of this sign in early diagnosis of gastric perforation following ulcer of the intestinal perforation in appendicitis or typhoid fever perhaps merits confirmation.

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**Total Leukocyte and Differential Counts in Typhus Fever.**—MATHES (*Münch. med. Wchnschr.*, Oct. 5, 1915) calls attention to the difficulty at times in distinguishing typhus fever from cases of typhoid fever with a very pronounced roseola. From his blood examinations he believes that a combination of total white count with a differential count will aid in quickly making a differential diagnosis in these cases. At first thought this would seem scarcely necessary, as most text-books

associate typhus fever with a high-grade polynuclear leukocytosis, usually 20,000 or above. The author studied the blood of 55 cases in which typhoid fever was excluded by the clinical course, negative blood cultures and Widal tests. 34 of the 55 cases had counts of over 10,000 but only 3 showed more than 20,000 cells per c.mm., and of these 3, 2 were fatal, while the disease in the third ran a very severe course. The average count was between 10,000 and 15,000, while in 8 of the 55 cases the total count was from 7000 to 10,000 and in 12 others it varied between 4000 and 7000. In most cases during the febrile period the polymorphonuclear neutrophile average was 80 to 85 per cent., while the eosinophiles are strikingly absent. During convalescence there is apparently a postinfectious lymphocytosis associated with an eosinophilia. During this period the neutrophiles fall to 50 to 60 per cent., while the lymphocytes rise to 40 to 50 per cent., and the eosinophiles from 5 to 9 per cent. The differential diagnosis from typhoid is difficult usually only in two types of cases; first, cases of typhoid associated with a leukocytosis of 10,000 to 15,000 such as has been noted by several authors in recently vaccinated people. In these cases the differential count shows a normal formula or a mononuclear increase instead of a polynuclear increase seen in typhus fever; the second difficult group includes the cases of typhoid fever with a leukopenia as was present in 20 per cent. of the author's cases. Here again the typhus blood shows a polynuclear increase instead of the usual lymphocytosis of typhoid.

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**Coagulation of Blood in the Pleural Cavity.**—DENNY and MINOT (*Am. Jour. Physiol.*, 1916, xxxix, 455) have made an experimental study of the fact noted clinically and experimentally that blood in the pleural cavity remains fluid or partially fluid and fails to coagulate after withdrawal. They summarize their findings as follows: Small amounts of blood introduced slowly into the pleural cavity when deep artificial respiration is maintained will remain in large part fluid. Small clots are always found in the pleural cavity, the size depending upon the amount of blood injected, and the rapidity of injection. The fluid portion of the blood can only be coagulated by the addition of fibrinogen. Thrombin, calcium and thromboplastin are incapable of causing coagulation. The blood shows absence of fibrinogen, which may perhaps be removed in some other way than by coagulation, but the authors found that pure fibrinogen solution which has been introduced in the pleural cavity under the same conditions not only is not altered but clots more readily than the control on adding suitable amounts of thrombin. Small amounts of thrombin and fibrinogen, however, when mixed in suitable proportions and injected slowly in the pleural cavity, remain fluid and show an absence of fibrinogen. Since it has been shown that fibrinogen solution loses none of its properties after remaining in the pleural cavity and that the presence of thrombin under the same conditions causes a disappearance of fibrinogen, we can only conclude, the authors say, that coagulation has taken place. The experiments with artificial solutions parallel those with whole blood, the conclusions being that blood which has been in the pleural cavity remains fluid, not because of any alteration of the elements, but because of previous coagulation and defibrination.

**The Present Status of the Abderhalden Reaction.**—In a very full article BRONFENBRENNER (*Jour. Lab. and Clin. Med.*, 1915, i, 79) reviews the present status of the Abderhalden reaction and the theory of the so-called "Abwehr Fermente." The technic of the reaction is gone over in detail and particular reference given to the possible sources of error and the methods for the preparation of the substrata. After the general discussion, the author comes to the following rather important conclusions. These are based upon a careful analysis of the literature and particularly upon work which he and his co-workers have carried out: (1) The serum ferments are not specific. (2) The dialysable substances originate not from the substratum but from the serum. (3) In-so-far as the test is specific, its specificity depends on the presence in the blood of substances identical with the antibodies and not specific ferments. Provided all the precautions prescribed are carefully adhered to and controlled, one may obtain satisfactory results in a number of cases. In a certain number, however, no matter how carefully the test is carried out, the results obtained are not correct. In its present form, therefore, the test undoubtedly requires that the men who perform it be thoroughly trained in serology as well as in the chemistry of enzyme action. Though the test remains comparatively useful in special cases and the results obtained may justify the expenditure of the time of a highly-trained worker, Brenfenbrenner still feels that the results thus obtained should be taken with great reserve until some method has been elaborated which will permit easy standardization of the substrata. At the present time the amount of substratum used in a test cannot be uniform in all cases, for different immune sera react with various amounts of substratum according to the amount of the specific antibody present. Moreover in the case of normal sera, the amount of substratum capable of inducing auto-indigestion, varies. As it stands at present, therefore, the Abderhalden reaction has only a scientific interest, and in that its main value is in the fact that it has stimulated the student of the fermentative activities of the body fluids and specially of the blood. The studies reported continue more and more to deny Abderhalden's basic contention, namely, that the body is endowed with the ability to respond with the production of a specific ferment upon the parenteral introduction of foreign substances.

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**Concerning Influenza.**—HUEBSCHMANN (*München. med. Wchnschr.* No. 32, 1915) made observations during an apparently typical epidemic of influenza in Leipzig. He considers the relation of the influenza bacillus of Pfeiffer to these epidemics and calls attention to the view expressed by some, that most of these epidemics of influenza are really due to the pneumococcus rather than the Pfeiffer bacillus which is present only as a saprophyte. Out of 110 cases studied, the true influenza bacillus was found in smears of the bronchial secretion 70 times, while it was present in pure culture in 30 cases. He concludes from his work that the true influenza bacillus of Pfeiffer was undoubtedly the cause of this epidemic. He emphasizes, furthermore, that the clinical picture is frequently that of a generalized infection and is not limited to the more common picture of a purely-localized, pulmonary disease. The relative mortality during this epidemic was stated to have been high but no actual figures are given.

## SURGERY

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UNDER THE CHARGE OF

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**A Contribution on Fractures of the Neck of the Femur Based upon Anatomical and Clinical Studies.**—LANG (*Deutsch. Ztschr. f. Chir.*, 1916, cxxxv, 101) says that it is useless to attempt to cure ununited fracture of the neck of the femur by wire sutures or bone pegs. The poor result is the unavoidable consequence of the anatomical conditions. The occasional bony union obtained is only the result of accident, and is due to the fact that the vessels running in the epiphyseal line were not destroyed. After suture of fractures in the middle of the femoral neck, bony union is almost sure to fail. Upon the basis of Lang's anatomical studies the best treatment is to extirpate the head of the femur. He found that the chief cause of pseudarthrosis, neoarthrosis, and shortening of the neck, was to be sought in the demonstrated poorly nourished femoral neck, since it is itself poorly provided with bloodvessels. The blood supply of the neck of the femur in adults depends upon two circulations. The number of bloodvessels in the one is limited. They run in the epiphyseal line and extend from there to the femoral head. The bloodvessels of the other circulation are abundant, break up into branches in the trochanteric fossa and extend from there into the lateral part of the femoral neck. Because the vessels of the median and lateral portions of the neck barely anastomose a considerable portion of the middle of the neck is free of bloodvessels. The Kocher method of extirpation of the femoral head is the only rational operative treatment of non-union of a fracture of the neck of the femur.

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**Ulcers, New and Old; Jejunal for Duodenal Ulcers.**—BLAND-SUTTON (*Lancet*, February 19, 1916, p. 387) says we know that chronic ulcer of the duodenum is a common lesion. For some undiscovered reason the ulcer in the majority of instances is situated within 2 cm. of the pylorus, and as a rule on the anterior wall of the duodenum, midway between its upper and lower borders. A chronic ulcer in this position is rarely accompanied by physical signs, but it sets up symptoms very easily recognized. Obstruction of the pylorus frequently complicates ulcers near the pylorus; it is caused by edema of the mucosa. This condition also occurs with an ulcer situated in the pyloric antrum. Some of the most troublesome ulcers in the pyloric region can neither be

seen nor felt in the course of a gastrojejunostomy. A small duodenal ulcer can only be detected when it involves the peritoneum and produces a tell-tale scar. The chronic ulcer of the duodenum is exceptional in another feature. It has never been proved that this ulcer has become cancerous. Bland-Sutton has long sought among the living, the dead, and in museums for a duodenal ulcer that has become cancerous; so far his search has been unavailing. Cancer arises in the duodenum, but not in the region that is the usual seat of ulceration. The frequency with which gastric ulcers become cancerous and the infrequency of cancerous change in duodenal ulcers are difficult of explanation. The jejunal ulcer that follows gastrojejunostomy, or the so-called peptic ulcer, causes pain in the epigastrium aggravated by the ingestion of food. The symptoms often resemble so closely those associated with a duodenal ulcer as to lead patients to complain that the pain and discomfort for which gastrojejunostomy was performed have returned. Since the treatment of duodenal ulcer passed into the province of surgery it has become the routine practice to perform gastrojejunostomy for its relief in the hope that by diverting the chyme through the new stoma into the jejunum the ulcer will heal. If the pylorus is obstructed by the ulcer the results are usually good, because the chyme must pass through the new stoma; but when the pylorus is patent the chyme flows through it and in some instances ignores the new route. The efflux can be watched with the help of an opaque meal and Roentgen-rays. Bland-Sutton believes it is better whenever practicable to excise the pylorus with the ulcerated portion of the duodenum and rejoin the stomach and duodenum on the principle of an end-to-end anastomosis. If this method could be made safe gastrojejunostomy for the relief of chronic duodenal ulcer with an unobstructed pylorus would soon be abandoned. Experience proves that posterior gastrojejunostomy with an obstructed pylorus is a beneficent operation, in spite of the risk the patient runs of getting a new ulcer for an old one. The new ulcer has been evolved in this generation by alterations in the environment of the jejunum brought about by surgery.

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**A Statistical Study of 539 Cases of Pott's Disease Treated by the Bone Graft.** —ALBEE (*Amer. Jour. Orthop. Surg.*, 1916, xiv, 134) sent a large number of printed question blanks to surgeons in this and foreign countries who had performed this operation. Thirty-three surgeons reported a total of 299 results, in 229 of which the disease was pronounced arrested; in 59 the condition was improved. Twelve of the 229 patients died, four of these fatalities being reported as due to shock. The remaining eight cases died in four months or longer after operation, either from complications or from intercurrent disease. Of the author's personal cases, only those that have been operated upon one year or longer are included in this report. There are 198 of these; in 181 the disease was arrested; in two there was improvement. To date, 12 have died. Six of these were entirely relieved of their Pott's symptoms and died of some intercurrent disease. Several cases operated on in other clinics have come under Albee's observation, in which a Roentgen-ray study has demonstrated that the graft was either too short, or was placed in the wrong vertebrae, or was so inserted

as to allow a lateral displacement of the graft. Every diagnosis of Pott's disease should be confirmed by a Roentgen-ray examination, which should include an anteroposterior view as well as a lateral or an oblique lateral. The disintegration and the crushing of the vertebral bodies should always be demonstrated before advising the operation. This is necessary not only to confirm the diagnosis, but it is most imperative to determine the number and the particular vertebrae involved, so that the graft can be correctly placed.

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**Cervical Ribs, Report of Seven Cases with One Operative Case.—**

PLUMMER (*Amer. Jour. Orthop. Surg.*, 1916, xiv, 146) says that cervical ribs have been observed as unilateral, or double, usually related to the seventh cervical vertebra, and varying in size and completeness from a fully developed rib with articulations and muscle attachments, down to a mere enlargement or overgrowth of the costal process of the vertebral unit. The commonest clinical evidence of the presence of the extra rib has been, in the cases recorded, a neural disturbance in the arm associated with pain, or pain and varying degrees of paralysis referable to the distribution of the ulnar nerve, and suggesting pressure on or injury to the eighth cervical root. Less frequently disturbances of the circulation of the upper extremity, and spinal deviations have been observed. Apparently the size and shape of the rib do not bear any definite relation to the intensity of the symptoms produced, as it has been noted that some of the larger ribs have caused little or no trouble, and in some of the bilateral cases the neural signs have been found on the side of the rudimentary growth.

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**The Conservative Treatment of Gangrene of the Extremities due to Thrombo-angiitis Obliterans.—**MEYER (*Ann. Surg.*, 1916, lxiii, 280) says that in cases of typical thrombo-angiitis obliterans, conservative treatment should be resorted to before amputation. The following sequence might be observed: (1) superheated air; best combined with (2) systematic hypodermoclysis of Ringer's solution. If these simpler conservative means prove of no avail, conservative operative measures are indicated, viz., (3) tying of the femoral vein or arteriovenous anastomosis. Both latter methods should be subjected to further careful clinical research as to their real value. Superheated air may bring improvement of the symptoms; however a lasting beneficial effect therefrom has hardly ever been seen. It rarely controls the pain. The systematic hypodermic injection of 400 to 500 c.c. of Ringer's (or of physiologic salt) solution (Mayesima-Koga) daily, or every second or third day, deserves a definite place in the conservative treatment of thrombo-angiitis obliterans. Its effect may be lasting or temporary. If temporary, repetition usually again brings improvement. Two such series of injections represent a sufficient test as to their fitness. If gangrene has set in, it can of course, not be made good. What has died remains dead. But its process may be stayed by the hypodermoclysis treatment; old and obstinate ulcerations may heal; the otherwise uncontrollable pain can be relieved. Internally, a simultaneous administration of organotherapeutic preparations deserves a careful test. Inflammation of the wall of the bloodvessels of the next higher groups to the capillaries, arterial as well as venous, seems to be respon-

sible for the thrombosis (Buerger). Its cause may be microbic. However, the increased viscosity of the blood, viz., blood that is thicker than normal, also seems to play an important role in the etiology of the disease. It is possible that an altered quality of the blood such as also represents a cause for the occurrence of the thrombosis and subsequent gangrene. On the basis of this reasoning, procedures which tend to reduce the coagulability of the blood within the body deserve to be tried in our efforts to find the underlying cause of the trouble. Intravenous injections of anticoagulating substances, as, for instance, of a 2 per cent. watery solution of sodium citrate, may prove to be a useful adjuvant to the systematic hypodermic administration of Ringer's solution.

## THERAPEUTICS

UNDER THE CHARGE OF

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**The Treatment of Typhoid Fever with Typhoid Vaccine Administered Intravenously.**—McWILLIAMS (*Med. Record*, 1915, lxxxviii, 648) has collected a total of more than 550 cases of typhoid fever treated with intravenous injections of typhoid vaccine and reported in the literature by various observers. In more than half of these cases the disease was cut short, the patient having been saved from one to several weeks of fever. McWilliams believes that a few deaths must undoubtedly be attributed directly to the injections of vaccine. However, this is likely to occur with any new and radical method of treatment. As the contra-indications and dosage are better understood, such deaths should become extremely rare. No one type of vaccine seems to possess any great superiority over other types with regard to treatment. The proper dosage for intravenous injections appears to be from 100 to 250 million bacilli. The injection of the vaccine calls forth first a marked leukopenia and several hours later a high-grade leukocytosis in typhoid patients. Variations in the number of polynuclear leukocytes are responsible for these changes, the lymphocytes remaining relatively constant. The eosinophile cells undergo an increase shortly after the injection. The various types of vaccine call forth similar changes in the blood picture.

**The Treatment of Typhoid Fever by Stock Typhoid Vaccine.**—WILTSHIRE and MACGILLYCADDY (*Lancet*, 1915, clxxxix, 685) report a consecutive series of 50 cases of typhoid in which two or more doses of vaccine were given for therapeutic effect. Seven of these patients died, giving a mortality of 14 per cent. Six of the fatal cases were complicated by severe bronchopneumonia, the seventh died from intestinal perforation at a period of the disease when it seemed as if the



vaccine had reduced the general typhoid toxemia. The authors divide this series into three groups according to the results of the treatment. In the first group, consisting of six cases, the vaccine did harm. In three of these the harmful effect was due to the doses being given with too short an interval (forty-eight hours) between them. These showed an increase of fever lasting for several days, but all eventually recovered. In the other three cases, bronchopneumonia occurred and seemed to be made worse by the treatment. The second group consisted of 12 cases, who were neither helped nor made worse by the vaccine. In 5 cases of this group the vaccine was given a thorough trial with no apparent effect on the course of the disease. In the remaining 7 the vaccine treatment was discontinued because of ensuing complications. The last group, 32 cases, showed benefit from the treatment. In 24 cases of this group a definite improvement began after the first or second dose and continued until recovery. Five cases showed no improvement until more than two doses had been given. In one case the vaccine was not used until late in the disease, but was followed by marked improvement. The two remaining patients responded well to the initial doses, but later doses seemed to coincide with relapses which ran their course unmodified by the treatment. The authors noted that the patients who responded best to the treatment seemed more prone to relapses, which, however, were not severe. They advise starting the treatment as soon as possible in the disease. They believe that a reasonable suspicion that a patient is suffering from typhoid is sufficient indication for beginning vaccine treatment. The initial dose is 250,000,000 and an interval of three days should elapse between doses. The second dose is 375,000,000, the third is 500,000,000 and following this each dose is increased by 250,000,000. Shorter intervals are not well tolerated, frequently tending to an increase in the symptoms. When a longer interval has elapsed if four days, the dose should not be increased, if over four days, the dose should be reduced. When a reaction was produced by the vaccine which was more than very slight, the same sized dose was either repeated or the dose was reduced. The vaccine treatment should be continued for ten days after the temperature is normal in order to avoid relapse.

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**The Efficiency of Various Antityphoid Vaccines.**—SAWYER (*Jour. Am. Med. Assn.*, 1915, lxx, 1413) says that the literature on antityphoid vaccination gives little information regarding its value under the conditions of ordinary civil life. To obtain information regarding the results of antityphoid vaccination in the civil population of California statistics were collected by Sawyer. He believes that the use of vaccine in civil life is a much more severe test of its value because the vaccine is most used when the exposure is greatest, and because only a small proportion of people in civil life are vaccinated. A total of 8124 persons received prophylactic inoculations and thirteen different vaccines of the several types in common use were employed. In the whole number of vaccinated persons, there were forty-one instances of true failures. All cases reported as typhoid fever and occurring at least thirty days and not more than two and one-half years after the first dose of vaccine were recorded as true failures. Most of the failures were in persons who lived in the same household with typhoid patients who had nursed

typhoid patients, or who had been exposed to some heavily polluted common food or water supply. Under such conditions of unusual exposure, the prophylactic use of vaccine seems to give an inadequate protection. Sawyer could determine little difference between the sensitized and unsensitized vaccines in common use as regards severity of reactions and the degree of protection obtained. A polyvalent sensitized vaccine supplied by the State Board of Health seemed to give slightly better protection, but the superiority was not conclusively demonstrated. Sawyer believes that widespread and severe exposures are prevented by better supervision over public water, milk, and food supplies, vaccination can be depended on to diminish greatly the residual typhoid fever, especially if a large enough proportion of the people are vaccinated to reduce contact infection to a minimum.

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**Therapeutic Typhoid Vaccination.**—REITER (*Deutsch. med. Wchnschr.*, 1915, xli, 1120) sums up his experience with typhoid vaccine as a therapeutic measure for typhoid fever. He says that in carefully and individually regulated dosage, typhoid vaccine, in the majority of cases exerts a favorable influence on the course of the disease. The vaccine tends to shorten the disease and lessens the mortality. The temperature is usually at a lower level in cases that react favorably to the treatment. If the temperature is not lowered by the treatment, the chances for benefit from the vaccine are slight. The action of the vaccine on the disease cannot be termed in any way specific. Complications of the disease do not seem to be prevented or benefited to any marked degree. Reiter believes that the results of vaccine treatment on the whole are sufficiently encouraging to add the treatment to the other measures that are usually used. While complications do not seem to be favorably influenced by the treatment, nevertheless they are not considered as contra-indications to the treatment with regard to dosage. Reiter believes that repeated small injections are preferable to single large doses.

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**The Etiology of Typhus Exanthematicus.**—The complete report of the etiologic studies on typhus fever by PLOTZ, OLITSKY and BAEHR (*Jour. Infect. Dis.*, 1915, xvii, No. 1) is taken up in three divisions. A. Bacteriologic Studies: A review of the literature and especially of the cross inoculations of Anderson and Goldberger indicates that the virus of typhus is present in the circulating blood during the febrile period; that it is non-filterable and therefore probably of microscopic size; and that it is probably of bacterial rather than of protozoan nature. Up to the present time, eleven cases of European epidemic typhus and forty cases of the local endemic form (Brill's disease) have been studied. The same organism was grown from seven of the cases of the European epidemic form and from eighteen of the cases of local endemic form. It is necessary to culture the organism anaerobically after the method used by Noguchi for spirochetes or by the method of Liborinus and Veillon. The organisms grow only in the deeper parts of the tubes and cultures are not considered negative until after twenty days. The organism grown is a small, pleomorphic Gram-positive bacillus which is non-motile, non-acid fast, not encapsulated, and producing no spores. Negative results are always obtained

on aerobic cultivation. Control cases cultured by the same methods gave invariably negative results. *B. Serologic Studies:* The biological reactions found with this organism, the authors feel, offer conclusive proof that Brill's disease (endemic typhus fever) and true epidemic typhus are identical. They have furthermore definitely associated this organism with the etiology of typhus fever. Complement-fixing bodies, agglutinins and precipitins are usually not seen at the height of the disease, but are present at the time of crisis, and increase during the postcritical afebrile stage. They can be demonstrated *in vitro* when the organism isolated from the blood of typhus patients is used as artificial antigen. The occurrence of these immunity reactions to the bacillus in question only in cases of endemic and epidemic typhus fever offers abundant evidence for its intimate etiological relation to the disease. *C. Experimental Studies:* These experiments have shown that an organism identical with that isolated from typhus patients can be isolated from animals (guinea-pigs and monkeys) to which the disease has been transmitted by inoculation of typhus blood. The number of bacilli in the circulating blood is directly proportional to the severity of the disease and greatest at the height of the febrile reaction. The number per c.c. of blood, however, is always small. It has been possible, furthermore, to reproduce the disease in animals by injection of the organisms isolated from the blood of human cases. The organism can again be recovered from these animals at the height of the disease.

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**Complement-fixation in Pertussis.**—OLNSTEAD and LUTTINGER (*Arch. Int. Med.*, 16, No. 1, p. 67) report the results of complement-fixation tests in one hundred and eleven cases of pertussis or suspected pertussis. They give an excellent brief review of the literature on this subject showing the marked discrepancies existing between the views of various workers, and offer as an explanation of these variable results certain minor differences in technique, such as methods of preparing antigen, amounts of antigen and serum used, etc. The primary objects if the investigation were to test the etiological relationship of the Bordet-Gengou bacillus and to determine the value of the complement-fixation test. About 40 per cent. of whooping-cough cases gave positive reactions with antigens of the Bordet-Gengou bacillus when inactivated serum was used. The highest percentage of positive reactions is given by convalescent vaccinated cases. A ++ reaction by inactive serum with an antigen of the Bordet-Gengou bacillus is diagnostic of whooping-cough. Any reaction less strong is only suspicious, while a negative reaction has no significance. From these results the authors conclude that the Bordet-Gengou bacillus is probably the etiological factor in the disease.

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**The Concentration of the Protective Bodies in Antipneumococcus Serum. Specific Precipitate Extracts.**—In connection with the finding of antisera for certain types of pneumococcus infection, CHICKERING (*Jour. Exper. Med.*, 1915, xxii, 248) has devised a method of concentrating the protective substances of the antiserum in a form containing but a relatively small amount of the serum proteins. The work is a direct sequence to a previous communication in which it

was shown that the immune substances of an antipneumococcus serum may be removed by specific precipitation with extracts of the proper strain pneumococcus. These precipitates were found to be protective for animals against many times the lethal dose of pneumococci. In the present communication the author shows that extracts of these precipitates will not only inhibit the growth of virulent pneumococci *in vitro*, but will also protect experimental animals as efficiently as does the original antipneumococcus serum from which they are made. Furthermore, these extracts contain only a minimal amount of protein and are consequently much less apt to cause the disagreeable features of serum sickness so commonly seen in patients treated with the whole serum. Evidence is also offered that these precipitates and extracts may produce an active as well as a passive immunity to pneumococcus infections in mice.

**The Treatment of High Blood-pressure.**—ELLIOTT (*Jour. Amer. Med. Assn.*, 1915, lxy, 999) believes that the most important measure in the management of high blood-pressure is the proper regulation of the personal habits and diet. He believes that vasodilator drugs serve a very useful purpose by modifying hypertension in the presence of certain complications, such as angina, apoplexy prodromes, stenocardia, and high tension headaches. Even as a routine they may occasionally prove of service, although in no instance should depressor effects be sought by the use of drugs alone. Much greater liberality in diet may be permitted non-nephritic cases than those of obviously nephritic type. Quantity is more important than quality in food selection. Provided renal function is well maintained, there appears no good reason why we should not permit a protein ration based on physiologic needs. The functional capacity of the kidney may be tested out with the phenolsulphonephthalein test. It has been asserted by Agnew, Folin and Denis and Seymour that, when the renal response to function testing falls to 40 per cent. or lower, waste nitrogen retention begins in the blood. Elliott reserves strict dietetic regulation for those cases showing a response of 40 per cent. or lower. In the routine observation of high blood-pressure, it will be found in the main that, for therapeutic purposes, the cases fall into two groups; those in which cardiac symptoms (dyspnea, angina, cardiac asthma, etc.) predominate, and those in which renal symptoms (polyuria, uremic manifestations, retinal developments, etc.) mark the case as plainly nephritic in type. The two groups require somewhat different handling. The renal type of case requires much stricter control of diet, greater care for elimination, and vigilant readiness to meet uremia emergencies. Uremia may develop as a steadily deepening chronic intoxication or as a sudden fulminating affair, appearing without warning or possibly precipitated by acute exacerbation of a more or less latent nephritis. Clinical observation alone may fail entirely to warn of the proximity of acute uremic developments. The greatest assistance may be derived from the routine employment of the phenolsulphonephthalein test. Cardiac failure may develop in either of two ways in arterial hypertension, that is, as left ventricular dilatation with falling systolic pressure and diminishing pulse pressure, or as a high pressure stasis with rising systolic pressure and pulse pressure maintained or increased. The

former type is characterized by relative mitral insufficiency and broken systemic compensation with edema, the latter by splanchnic stasis, gallop rhythm, medullary dyspnea, often without edema and without heart murmurs. High pressure stasis calls for free hydragogue catharsis, perhaps bleeding, the type of left ventricular failure demands neither of these measures. They both require digitalis stimulation. The author emphasizes the point that digitalis is the most useful drug that we possess in high blood-pressure of whatsoever origin. It acts just as well and even better with a high pressure than with a falling pressure. Indeed, it will lower a rising pressure, and raise a falling pressure, provided cardiac embarrassment is the underlying cause. His experience leads him to urge that digitalis be employed early at the very appearance of cardiac decompensation, and it should be continued until thorough compensation has been reestablished. If administration by mouth fails to secure the proper effect it should be employed intravenously. Strophanthin in sterile solution by intravenous administration is a highly efficient preparation in the heart failure of high blood-pressure. One-half cubic centimeter of 1 to 1000 solution of strophanthin injected into the elbow vein at appropriate intervals for several doses will often induce cardiac reaction when other measures fail. After the effects become apparent, digitalis may be substituted and the effect continued.

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**The Treatment of Nephritis.**—PHIPPS (*Boston Med. and Surg. Jour.*, 1916, clxxiv, 73) says that during the past three months he has tried administering thyroid extract in the treatment of nephritis. Although his results were not uniform and although the study of the patients was necessarily incomplete in some instances, yet almost every case showed certain phenomena which were notable and at least suggestive of beneficial results of the medication. Phipps cites a few typical cases, and noted a particularly favorable effect upon edema. One case recovered from uremia, whereas he had been growing steadily worse and apparently was moribund until thyroid extract was added to his treatment. Cases of nephritis associated with hypertension were favorably influenced both as regards their hypertension and other symptoms of their disease. Phipps advises caution in administering thyroid extract and believes that if given carefully the administration of the drug is safe. He is of the opinion that thyroid medication should be given a more extended trial in nephritis.

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**The Allen Treatment of Diabetes.**—BOOKMAN (*New York Med. Jour.*, 1915, cii, 1240) reports his experience in treating 24 cases of severe diabetes by the starvation method of Allen. His results agree with those of Allen and of others who have used this method. The patients rapidly become sugar free, and with few exceptions have improved in every way. The results in the juvenile cases have been most convincing. The author believes that in the management of severe diabetes the Allen method is a great step in advance, that it brings excellent results and brings them quickly. He finds this method perfectly feasible under the ordinary condition of private practice.

## PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M.D.,  
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**Diagnostic Phenomena of Infantile Weak-mindedness.**—A. W. LIVES (*Pediatrics*, 1916, xxviii, 67) aptly points out that a newborn baby corresponds in every sense to our definition and comprehension of idiocy since it lives reflexly and automatically and with this the as yet undeveloped brain has nothing to do. While the infant then cannot be called weak minded, an imbecile or demented, the mind being undeveloped, yet in the rapid development occurring subsequently certain retardations and signs presage the future accomplishment of these states of weak-mindedness. Retarded mental development may be due to simple evolutionary defect in quantity or quality or construction of the brain; to mental defect from intra-uterine disease such as meningitis or to hemorrhage from prolonged labor or pressure or to lack or perversion of internal secretions. These defects through inadequate reflex response cause a deficiency of spontaneous attention, hence the earliest diagnostic symptom of impending phrenasthenia is lack of attention. There is failure to notice things, an early indefinable tinge of physiognomy, a lack of expression or vacuous stare and something unnatural in the child's movements which presages future calamity. It is important to remember that all this may be due to congenital blindness and deafness. This lack of attention to external stimuli points to abnormal brain development, and resultant feeble-mindedness. The special senses of taste and smell and touch are acute from the first day in normal infants and indifference to bad odors or sour tastes or backwardness in nursing suggests blunting of the senses. Weak-minded children may remain unduly still as in cretinism or be in constant rhythmic motion as in the mongolian type. Anatomical anomalies of all kinds are significant in direct proportion to their number and prominence. Cretinism with its characteristic signs is seldom recognized before the sixth month while the mongolian type is often recognized a few days after birth. Frequent causeless crying and screaming and uncouth sounds generally prognosticate later mental deficiency. Impending idiocy makes itself felt during the early months of life, imbecility not until some years have passed. Hereditary insanity generally first shows itself about the age of puberty. About 20 per cent. of these defectives are hereditarily luetic. Early diagnoses of mental deficiency are essential to the proper care and treatment of those affected and from the economic and communal importance of hereditary transmissibility of these mental defects.

**Myotonia Congenita (Thomsen's Disease) in a Child.**—JOHN THOMSON (*Edinburgh Med. Jour.*, 1916, xvi, 216) in discussing this condition in a typical case says the great degree of muscular hypertrophy shown is characteristic of cases where the disease develops

early in life. It is such a striking feature that it is apt to lead to a mistaken diagnosis of pseudohypertrophic paralysis. The prognosis of myotonia congenita is very different, however, as the abnormality of the muscles is unlikely to increase in later life and the patient, although probably always handicapped in his movements may be expected to acquire increasing skill in managing his unruly limbs. The case reported occurred in a boy, aged six years, the complaint being slowness of opening the eyes from earliest infancy and stiffness in the lower limbs ever since he began to walk. His intelligence has always been above the average and the thoracic and abdominal organs are normal. The difficulty in opening his eyes quickly is striking but readily passes off when the action is repeated several times. A similar slowness is noticed in the descent of the upper eyelids on looking down. The voluntary muscles all over the body, including those of the hands are much larger and stronger than those of a normally developed child. They show the same deliberation in contraction as the muscles of the eyelid when an attempt is made to bring them suddenly into action after a period of rest. A portion of muscle excised for pathological examination showed as the outstanding feature "a marked nuclear increase (sarcolemma nuclear proliferation). The muscle fibers are also slightly enlarged and the longitudinal and transverse striation is slightly more evident." There has been no trouble with micturition and enlarged tonsils and adenoids were recently and successfully removed under an anesthetic.

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**Prevention of Heart Disease in Rheumatic Children.**—C. O. HAWTHORNE (*Amer. Med.*, 1916, xi, 99) points out that in rheumatic fever of adults joint symptoms are common and cardiac lesions occasional, while in children suffering from this disease arthritic incidents are inconspicuous and the risk of heart complications is very pronounced and heart lesions are a common result. One reason for this apparent cardiac susceptibility in rheumatic fever is probably the absence of painful joint symptoms in children with a consequent neglect of early and complete rest which would save the heart, and which is imposed on the adult by the painful joints. It is in this direction we must look for the prevention of cardiac mischief in children by securing the protective influence of early and complete rest. The medical profession is responsible for the proper education of families in the significance of a rheumatic inheritance on the children of the families or where a valvular condition has developed in one child to protect the others in similar cases of illness by early and complete rest. If the method proposed here does not seem to offer a very large promise, yet it has no competitor and until an alternative is proposed it is the plain duty of the profession to utilize it.

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**A Criticism of "Whole Milk" Feeding.**—ERIC PRITCHARD (*Amer. Med.*, 1916, xi, 19) offers the following reasons against the policy of "whole milk" feeding in infants. He agrees that while in general the method gives good results it does not give "the best" results. It is unwise to confine oneself to any one particular food or method of feeding. It makes little difference what food one employs provided the following essential conditions are complied with: (1) the necessary elements for growth, maintenance, heat and energy production must

be supplied in quantities required in each particular case; (2) these elements must be presented in a digestible and assimilable form and suited to the special physiological make-up of the child, and (3) the food must be of such a nature as to exercise and develop latent digestive capacity. Instead of modifying the specific physiological make-up of a child to a certain kind of food, a task which is very often impossible, Pritchard believes in adapting the food to physiologic idiosyncracies found in every case. Food requirements can be approximately estimated in terms of calories and on a basis of weight and age and, further, a mixed diet of proteins, fats and carbohydrates is better for a growing baby than any one or two of the proximate principles without the others. Dr. Vining's figures on the relative proportions of the elements of human and cow's milk are incorrect and Pritchard places the difference in the amount of lactose at 25 per cent. instead of 10 per cent., and in the amount of protein at 100 per cent. to 150 per cent., instead of less than 10 per cent. This is the central argument against the substitution of the one milk for the other in infant feeding. A food adaptable to a three months' infant should yield 495 calories and contain the three elements in the proportion found in human milk. The dilution of infants' food is too often excessive, the success of the "whole milk" method being probably based on the limited quantity of water used in that method. Individual adaptation is essential to the successful administration of food to infants and it is believed impossible for the physician to recognize pathological manifestations and modify the food accordingly if his practice is confined to one method of feeding. If the principles of percentage feeding are understood synthetic foods can be prepared in many ways to satisfy different physiological requirement. Dried milk if properly modified has all the advantages and few of the disadvantages of so-called dairy milk.

## OBSTETRICS

UNDER THE CHARGE OF

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**The Nourishment and Care of Prematurely Born Children.**—LANGSTEIN (*Berl. klin. Wchnschr.*, 1915, No. 24), reports the results of methods in use in the Empress Augusta Victoria Hospital for infants in Berlin. Among the inmates were 250 prematurely born children. Formerly it was customary to keep these in an incubating room whose temperature varied from 80° to 90°, and where the air contained 60 per cent. of moisture. There was reason to believe, however, that children kept in this room were less robust and developed less rapidly than those brought outside and given a better atmosphere and, accordingly, the use of the room was abandoned. The writer kept these prematurely born children in an ordinary nursery and supplied artificial



warmth as needed for each child. The apparatus employed was one which used circulating hot water as a source of heat. In feeding children, the best method consisted in introducing food into the stomach through a small stomach-tube and very small quantities of milk were employed in feeding, the quantity increasing gradually but steadily. After two weeks of such care the infant was usually able to drink. Prematurely born children were fed about every two hours or at least given nine or ten feedings in twenty-four hours. When there was no mother's milk available to introduce through the tube, modification of cow's milk diluted with water and containing sugar and with a considerable fat percentage were employed. In some infants, mixtures which contained some percentage of a cereal material with sugar proved advantageous. All prematurely born children showing a tendency to rachitis and spasmophilia should be given preparations of calcium against such dangers. Calcium phosphate or calcium lactate or tricalcol in combination with cod-liver oil gave especially good results. As early as possible, small doses of iron were given, if examination of the blood of the infant showed that as early as the second or third month of extra-uterine life, symptoms of anemia had developed. A good prognosis for the child may be given when at from six and a half to seven months the child weighs 1000 gms. and is 34 cm. long. It is evident that the induction of labor in contracted pelvis may be resorted to without benefit if adequate precautions be not taken to care, after its birth, for the prematurely born infant.

**Shall More than One Finger be Employed in Vaginal Examination in Parturient Cases?**—In the effort to lessen danger through vaginal examinations, AHLFELD (*Monats. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 6), has criticised the introduction of more than one finger in such examinations and the method described by Schultze in his textbook and by others as well. His printed instructions were intended especially for midwives and Schultze reviews his instructions, which certainly indicate no lack of precaution in the matter of asepsis. The discussion seems a very small matter, and yet it is evident that the omission of thorough vaginal examinations may become a danger to the patient unless practical and not theoretical methods prevail. If antiseptic precautions be honestly and thoroughly carried out, and sterile gloves be employed, it were far better that the entire hand, if necessary and possible, be introduced and a thorough examination be made than that a false diagnosis resulting in harm to the patient should result because but one finger was employed. SCHULTZE (*Monats. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 4), takes this view and makes a point in favor of a sensible and practical technic very clear in his timely communication. His warning is especially timely in all cases where there is delay in labor. In such, unless the head has become well engaged, the pelvis should be palpated by as many fingers as can be safely introduced. In this way important pelvic abnormality will be discovered, the nature and exact position of the presenting part, its relation to the brim and to the lower strata of the pelvis, the presence or absence of flexion, and descent and rotation. Unless a thorough examination be made it is quite possible for the cord to prolapse but a short distance and this loop to become pinched between the head

and the pelvic brim, resulting in the death of the fetus, when a superficial examination with one finger might not detect the presence of the prolapsed cord and thus fail to arouse the obstetrician to appropriate efforts to save the life of the infant.

**Pelvimetry by the Roentgen Rays.**—RUNGE and GRUENHAGEN (*Monats. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 4), reviews several of the methods for measuring the pelvis by the Roentgen rays and describes a method which they have found valuable. This consists in determining certain points of the pelvis by the ray and then by algebraic formulae, obtained by previous examination and calculation, working out the proportions of a given pelvis. The method is illustrated by equations and by geometrical figures. It should prove of interest to all those who are concerned in the mathematics of modern pelvimetry.

**Complications Arising during Labor through Maldevelopment of the Uterus.**—VAN DE VELDT (*Monats. f. Geburtsh. u. Gynäk.*, 1915, Band xlii, Heft 4), recognizes what he terms uterus micornis through failure in one of the Müllerian ducts to completely develop. This deformity is not very frequent and has little comparative importance so far as practical obstetrics is concerned. Double uterus and vagina are not exceedingly rare and uterus duplex is double development of the uterus only. Further, there may be two uterine bodies and but one neck and again the uterus may be cordiform where the fundus is somewhat flattened and the uterus assumes an irregular heart-like shape, though there may be a double uterine cavity with greater or less extent of the dividing partition, and again, this dividing partition may be in different portions of the uterine extent. In labor, we recognize the complications arising from a defective development of the uterus, as in infantile uterus and hypoplasia, and we also note that complications in labor may occur through congenital anomalies of the cervix. Cases where difficulty in labor occurs through uterus unicornis are not often observed. Moldenhauer reports a case of labor in which a premature fetus was found in the upper portion of a uterus apparently enclosed in a thin-walled sac, which had posteriorly an opening about the size of a silver half-dollar through which membranes and placental mass were protruding. It is interesting to observe that the placenta had attached itself to the weakest portion of the uterus. In cases of double uterus, labor may be complicated and delayed by that portion of the uterus which has not been pregnant. Raynes described a case before the Obstetrical Society of Paris where the vaginal portion of the pregnant uterus was very high in the pelvis and directed toward the right of the median line. The patient was evidently a primipara, the vaginal end of the uterus somewhat shortened and the os closed. By ballottement, one could obtain the head very high through a thin lower uterine segment; the fingers could not reach the promontory. In the left quadrant of the pelvis one found a small semi-hardened mass whose nature it was difficult to determine. This subsequently proved to be the unimpregnated half of the uterus which had become so wedged into the pelvis as to hinder the descent of the fetal head in the pregnant portion of the womb. That a uterus duplex may occasion difficulty in labor has been illustrated by STAHLER

(*Zentralbl. f. Gynäk.*, 1906, No. 2). His patient has premature rupture of the membranes and pain at intervals for twenty hours resulting in the complete dilatation of the cervix. Presentation was breech but the child showed no tendency to descend into the pelvis. As uterine pains were good, the force of the uterus seemed to be directed rather against the left side of the pelvis than in its axis. The effort was made by placing the patient upon the left side, to bring about a better application of force, but this did not succeed. Often in multiparous patients, a combination of weakness of the uterine muscle itself, expulsive segment and rigidity of the cervix produces the complications in labor which predispose to rupture of the uterus. Gosset and Tissier reported before the Obstetrical Society of Paris, 1906, a case in which the patient died during labor from hemorrhage from rupture of the lower uterine segment with the anatomical conditions just described. Somewhat similar in effect are those cases of atresia of the genital tract, either acquired from preëxisting inflammation or congenital where the anatomical conditions predispose to rupture of the uterus. The reviewer recently saw a case of uterine rupture in a multiparous woman who entered the examining-room of a large general hospital for admission in labor. While making her application, the membranes ruptured and considerable amniotic fluid escaped. She was then transferred to a maternity department. On admission the abdomen was large, fat and flabby, its contour indefinite, the exact contour of the uterus and the position and presentation of the child could not be made out. Fetal heart sounds were not heard. On vaginal examination, the vagina was full of clotted blood. When this had been washed away by a lysol douche, the cervix was resisting, thickened, admitting three fingers. The placenta was attached at the edge of the external os and had partly separated, which accounted for the hemorrhage. The child lay obliquely across the pelvis, an arm had partially prolapsed. The patient had had several strong uterine contractions and the uterus was so tightly closed upon the child that efforts to perform version would have been exceedingly dangerous. In addition to the complications described, examination also disclosed a transverse rupture through the lower uterine segment about two inches long on the posterior aspect of the uterus. As soon as possible, the abdomen was opened and the Porro operation was performed. The rent in the lower uterine segment was closed, leaving however, room enough in the middle for a gauze drain which was passed through from the pelvis into the cervix and vagina. The patient was severely shocked, requiring transfusion and other stimulation, but rallied successfully from the operation. Van de Velde describes the case of a patient, aged twenty-nine years, pregnant for the first time, who came to labor at term, but the attending physician could not recognize a normal condition of the cervix and could not make out the fetal presentation. The contraction ring was high and the axis of the uterus extended obliquely across the pelvis. In the region of the lower uterine segment there was great tenderness. On vaginal examination, the finger could make out that the fetal head was in the pelvic cavity and the sutures could be recognized indistinctly through the distended uterus. No opening in the uterus wall could be made out and when the patient was anesthetized and specula used, it was still impossible

to find the os uteri. On the right side and high up behind the pregnant uterus could be felt a vaginal portion of the cervix and the os, through which a finger could be inserted. On repeated examination under anesthesia the finger could be inserted to the fundus of this small uterus, which was thus proved to be empty and not in a pregnant condition. The vagina and perineum were incised and vaginal cesarean section was performed. The bladder was drawn high up. It was difficult to push it aside. The abdominal cavity was not opened; the membranes protruded and were easily ruptured and a medium-sized living fetus was removed by forceps. The placenta was delivered manually; the uterus tamponed with iodoform gauze and ergot given hypodermically. The incisions were closed with catgut and an opening left into the uterus for drainage. The patient made a good recovery and was shortly after pregnant for the second time in the right uterus, which aborted about the third or fourth month, and after this, again in the left uterus, the child being born living, but dying soon afterward and evidently premature. The patient then had a tuberculous peritonitis, from which she recovered after section. On opening the abdomen, both Fallopian tubes were found covered with small tubercles and consequently were removed. There seemed to be two uteri smaller than normal joined together at the lower portion at the cervix and diverging in the bodies. The urinary bladder lay between the two corpora and behind both cervices. On vaginal examination both cervices could be detected and it had been observed that during menstruation blood issued from both of the uteri. Various authors describe differently the uterus which apparently has no cervix and no os uteri which can be found at the time of labor. In some, the case described by Van de Velde would serve as a type; in others there is no double cervix, and the condition would be best described under the term atresia. Usually by careful examination, one can detect the opening of the cervix and, taking this as a guide, open the uterus by some form of incision. A case of this sort came under the observation of the reviewer when summoned by two physicians in consultation over a woman in labor, who had vaginal hemorrhage and in whom the physicians could not find the cervix or os uteri. On careful inspection, the uterine tissue was greatly distended and very thin and was beginning to tear transversely and blood was issuing from the extending laceration. By placing the patient in the left lateral position and withdrawing the perineum and using a strong light, a very small aperture could be found through which a grooved director could be passed. This was taken as the rudimentary os and was cautiously enlarged until the finger could be inserted, when it was stretched sufficiently so that from this point multiple incisions could be made, opening the cervix freely. The child was then delivered by forceps, the uterus emptied and packed with gauze and the cervical lacerations closed throughout a considerable extent with catgut. Van de Velde calls attention to the fact that in such a case it would be a mistake to deliver the patient by abdominal cesarean section because no adequate aperture would be left for the discharge of the lochia. Vaginal cesarean section he believes to be much safer and indicated in such a case.

**Tiflitis and Peritiflitis Complicating Pregnancy.**—JAECHSKE (*Zentralbl. f. Gynäk.*, 1915, No. 37) describes the case of a primipara, aged twenty-six years, who, during the preceding two years had several attacks of irritation in the region of the appendix which led her family physician to advise the removal of the appendix. This was not done and pregnancy proceeded apparently normally until three weeks before term. The position and presentation of the fetus became abnormal. The patient was sent to hospital with the history of two days before having considerable fever which was thought to result from an attack of influenza. Improvement was followed by higher fever and the physician summoned sent the patient immediately to the hospital. On admission her temperature was  $104.5^{\circ}$ , pulse 104, of good volume and tension, the tongue was coated and moist, the patient complained of nothing and there were no labor pains. No pathological condition could be found in the neck, mouth, lungs or heart. There was slight tenderness over the region of the right kidney and tenderness in the abdomen over the appendix, although it was not well marked. The urine showed abundant leukocytes and some albumin. The question of pyelitis from colon bacillus infection of the right kidney was considered, but the symptoms were thought to point more to appendicitis or possibly a beginning typhoid. Examination of the blood showed 17,000 leukocytes and this led to a diagnosis of appendicitis. Two hours later the tenderness of the region of the cecum had increased considerably and soon after an operation was undertaken. On making an incision in the right lower abdomen thin pus escaped from the abdomen in a stream. This was allowed to escape and a packing of gauze introduced and then with fresh instruments and disinfection a vaginal cesarean section was performed and a dead child delivered by version. After the conclusion of this operation, abdominal section was completed. It was found that an abscess had developed, one wall of which was composed of the right broad ligament and pelvic tissues, the other portion of adhesions and the surrounding intestines. The appendix was thickened and edematous and markedly injected and kinked at its base, the free end of the appendix lying in the region of the ovary. No perforation could be made out. The cecum over an extent of 5 cm. was edematous, covered with a foul grayish red exudate. On the posterior surface of the cecum there were ulcerated surfaces. The free border of the right ovary formed part of the wall of the abscess and although the right Fallopian tube was reddened the right orifice was patent. The uterus was well contracted. Three gauze drains were carefully introduced, one of them covered with sheet rubber and the abdominal wound was left open. The patient was placed in Fowler's position and Ringer's solution was introduced by the drop method into the bowel and 1 c.c. pituglandol was injected into the muscles four times daily. This patient died on the fourth day from acute diffuse peritonitis. An autopsy was obtained. In the pus were found the colon bacillus and hemolytic streptococci. Microscopic examination of the appendix showed its mucous membrane intact throughout but the tissues were edematous and swollen with free multiplication of round cells. In reviewing the case, it was impossible to demonstrate the initial point of infection. That the colon and the tissues about the colon were involved was evident, but, in the absence of perforation of the appendix, it was difficult to trace the course

of the infection. The reviewer had occasion to open the abdomen of a young primipara who had suffered from fever after childbirth with indefinite symptoms. Typical puerperal sepsis could be excluded. There was diffuse abdominal tenderness without fixation of the uterus and without a definitely localized painful point upon pressure. The appendix was found reddened, thickened, edematous and without perforation. At the beginning of the descending portion of the colon beneath the peritoneal covering were several areas of laceration which could be plainly made out. The entire colon was larger than normal, reddened and the lymphatics leading from the colon were enlarged. There were some recent and light adhesions between coils of intestine and the omentum. A Mickulicz bag was introduced into the bottom of the pelvis and the upper portion of the wound was closed. The patient made a tedious but complete recovery. In this case, the Widal reaction was negative, the urine was free from colon bacilli and the case was considered one of colon bacillus infection of the appendix and bowel itself. The appendix was removed and on examination found to contain colon bacilli and to be in a condition of acute inflammation.

## OPHTHALMOLOGY

UNDER THE CHARGE OF

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**Effect of Accommodation upon the Viscosity of the Lens.**—LANCASTER and WILLIAMS (*Ophthalmoscope*, March, 1915, p. 112) have made a series of experiments upon the position of the punctum proximum, from which they infer that, when during accommodation the zonula is relaxed, there is an initial change which occurs quickly (less than a second), but that the effect does not stop there, the lens continues to become more convex, though at a slower and slower rate. They believe that the force which brings about the increased convexity of the lens is opposed by another force which it overcomes only gradually. There is a time element. They call the first force the elasticity of the lens, capsule, etc.; for the second they suggest the name viscosity, for the time element is the essence of viscosity.

**Complete Disappearance of an Eyeball following a Birth Injury.**—HARDY (*Amer. Jour. Ophthalmol.*, February, 1915, p. 33) observed, in a child of eight years, an empty socket exactly like that resulting from an ordinary enucleation; its depth in fact was somewhat greater. The mother when questioned made the surprising statement that no operation had ever been done. The eyeball had been injured at birth by the

forceps, and according to her understanding, the globe had been ruptured, which rupture must have occurred posterior to the cornea, as from her statement, iris and cornea had the same appearance as the other eye. No stump or remnant of the globe could be seen or felt at the apex of the orbit. The eye had completely disappeared. All the evidence was against an ophthalmia. Complete absorption of every part of a perfectly formed eye even after a destructive injury at parturition is, to say the least, an extraordinary occurrence.

**The Use of Optochin in Various External Diseases of the Eye.** — STENGELE (*Klin. Monatsbl. f. Augenheilk.*, April-May, 1915, p. 446) reports upon the extraordinary curative effects of this agent in certain diseases of the eye, especially pneumococcic infection, diseases of the lacrimal sac and affections in which photophobia is favorably influenced by the remedy. As usually employed in 5 per cent. solution, it is apt to be very unpleasant even increasing the irritability of the eye for a short time; such irritation may be prevented by a prior instillation of a 5 per cent. solution of cocain; in 1 per cent. solution it is borne alone without cocain. Fresh solutions or those a few days old, are more efficient than older ones; solutions three to four weeks old are almost inert. Optochin is a new quinin derivative known scientifically as ethylhydrocuprein. Corneal ulcers from pneumococcic infection treated every hour or two by 1 per cent. solution of optochin yield surprisingly rapidly to the remedy. The same agent is of great service in corneal ulcers accompanied by disease of the lacrimal sac. The instillation of a 1 per cent. solution of optochin into the conjunctival sac in combination with injection of the lacrimal passages with the same agent simplifies the treatment very decidedly. The secretion of the blennorrhea of the lacrimal sac rapidly ceases so that extirpation with subsequent bandaging can be safely performed. But irrigation of the passages with optochin can not replace extirpation in ectasia of the sac; sooner or later renewed infection will require operation. The effect of the drug in 5 per cent. solution is truly surprising in the various external ocular diseases, especially serofulous ophthalmia. It is astonishing how children who have been unable to open their eyes for days and weeks, quite suddenly open them freely, and the photophobia is permanently relieved after a short period of treatment. The drug may act slowly and may even fail entirely in such cases of phlyctenular disease as are complicated by fissures of the external canthus; the latter should be brought to heal before the application of the optochin. It is an interesting question how this drug relieves photophobia so promptly in some cases and fails in others. Stengele ascribes the curative effect to its bactericidal action and not to simple anesthesia as has been assumed. It is a matter of further investigation to determine against which species of bacteria besides pneumococci the drug is effective.

**Interesting Note upon the History of the Fundus Reflex, Bearing upon the Invention of the Ophthalmoscope.** Helmholtz in his monumental work *Physiological Optics*, first published in 1856, and also in his *Description of an Ophthalmoscope* in 1851, and Mauthner likewise in his *Ophthalmology*, 1868, ascribed priority in the matter of

researches upon the fundus reflex as bearing upon the invention of the ophthalmoscope to Cumming, 1846, and von Brücke, 1847, and the host of subsequent writers upon the ophthalmoscope without exception have repeated the statements of these masters. HIRSCHBERG (*Centralbl. f. prak. Augenh.*, April, 1915, p. 81), that most erudite historian of ophthalmology, calls attention to a passage in a small work in Latin by Purkinje, published in 1823, in which he not only describes the reflex as visible by light reflected from his own myopic lenses (he was himself myopic 6D) into the eyes of a dog and also of man, but actually examined the fundus of a model eye which he constructed, filled with clear and turbid water, and recommended the method for practical diagnostic purposes. But a lifetime had to elapse before his recommendation bore fruit. In this respect, the lot of Purkinje resembled that of one still greater, Thomas Young.

**Synchysis Scintillans.**—WESTPFAHL (*Arch. f. Augenh.*, 1915, lxxviii, 1) analyzes 40 cases of this affection observed in the Würzburg clinic. In 36 the condition was unilateral. Its character as a mark of degeneration was shown both by its occurrence in advanced years with other senile changes, and from the circumstance that when it occurred earlier, it was accompanied by degeneration of other portions of the eyeball (retinal detachment, phthisis bulbi). In about half the cases the fundus was normal and the visual acuity good; this excludes any toxic action of cholesterol products which may be present in the vitreous, upon the retina; 25 per cent. of the cases showed more or less advanced senile opacities of the lens, although this may have been a coincidence as the average age of the subjects in this series was seventy years, while the average age of all the cases of synchysis was sixty-four years. Of the remaining cases in which the synchysis was accompanied by some other internal disease of the eye, the latter could be regarded as the cause of the vitreous opacities in less than half.

**The Intra-ocular Pressure and Tension of the Eye.**—In a lengthy publication upon the above subject, running through three numbers of the *Ophthalmoscope* (from April, p. 182, through May, p. 237, and concluded in July, p. 327), ELLIOTT summarizes his conclusions as follows: 1. In dealing with the physical conditions governing the behavior of the intra-ocular fluid, as it passes into and out of the eye, it must be borne in mind that we are dealing with a body of "moving water," and that the laws which come into play are those of hydrodynamics and not those of hydrostatics. 2. The question whether the intra-ocular fluid is poured out by an act of secretion, or by a process of pressure filtration is still sub judice; probably both take part. The question, however, is not of great practical importance. 3. The general blood-pressure, as it rises and falls, tends to exert a corresponding influence upon the intra-ocular pressure. This influence may, however, be masked or even counteracted by a number of other factors. 4. The venous exit pressure throughout the eye is probably always a little in excess of the intra-ocular pressure. 5. The most probable explanation by which the intra-ocular fluid finds its way into the canal of Schlemm and into the veins of the iris is that the action is osmotic in nature although there are difficulties in understanding the problem in all its bearings.



**Does Sympathetic Amblyopia Exist?**—This term has been employed to describe what has been regarded as a purely functional weakness of vision of one eye occasioned by conditions of irritation in the other and which disappears upon cessation of the latter. A number of such cases have been recorded in literature. KEUTEL (*Klin. Monatsbl. f. Augenh.*, Feb.-Mar., 1915, p. 250) subjects 25 of the most striking cases to a critical review from which he comes to the conclusion that none of them can withstand thoroughgoing criticism. He maintains that sympathetic ophthalmia does not exist and that the expression should be stricken from ophthalmic terminology. Those cases where, following enucleation, the visual acuity rapidly improves, are explicable in the majority of cases by the circumstance that the irritative symptoms—photophobia and lachrimation—disappear, symptoms which influence the visual acuity mechanically or functionally; or else suggestion plays its important part in bringing about a rapid improvement of the visual acuity with the accompanying contraction of the fields.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Caseous Tuberculosis of the Aorta.**—ZRUNEK (*Cent. f. Path.*, 1914, xxv, 577) reports a case of false aneurysm of the abdominal aorta. This was found in a woman, aged twenty-seven years, in the region of the celiac axis. The aneurysm was of large size and projected between the stomach and liver. The aneurysmal sac was mainly composed of a fibrin clot contained within a thin sheet of tissue which had ruptured at one point, with extensive hemorrhage in the abdomen. About the communication between the aorta and the aneurysm the tissues were involved by caseous tuberculosis. The tuberculous process had attacked the aorta from without, probably by invasion from neighboring lymph glands. Curiously, a miliary tuberculosis was present only in the liver and spleen.

**Concerning Substances Inhibiting Coagulation Found in the Placenta and Female Genitalia.**—Many explanations have been given for the lessened coagulability of the menstrual blood. FRUCH (*Biochem. Ztschr.*, 1914, lxi, 368) has again studied the subject from the attitude that the coagulation property of the blood is inhibited, rather than, as is

suggested by some, that certain constituents necessary for coagulation are lacking. He found in his experiments that the uterus, tubes and ovaries of woman contained substances antagonistic to fibrin ferment. The ovary was particularly rich in these substances. Their presence had no particular relation to age, and may readily be removed from fresh tissues. The author was unable to support the finding that the placental tissues contained accelerating substances for coagulation. Fugii found that extracts of placenta equally inhibited coagulation as did the tissues of uterus and ovary. It is suggested that possibly the property of the placenta is a factor in preventing intra-uterine placental thrombosis as well as in assisting an interchange of maternal and fetal fluids.

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**Multiple Pseudocysts of the Peritoneum Associated with Colloid Cancer and Ovarian Teratoma.**—Pseudocystic masses are not uncommonly found implanted on the peritoneum. These may have different modes of origin. Some arise through the encapsulation of mucinous materials which have escaped from ruptured cysts or occur as secondary newgrowths where particular types of cancer cells have been implanted upon the peritoneum. Occasionally, too, rupture of ovarian dermoids may lead to encapsulation of fatty material with cyst formation. ROTH (*Ziegler's Beiträge*, 1915, lxi, 42) described a typical case of colloid cancer of the colon with numerous metastases in the liver and peritoneum. The peritoneal nodules were partly true secondary growths while others were merely masses of colloid lying upon and partially organized by the peritoneum. The quantity of free colloid material was quite remarkable. This free colloid contained no evidence of epithelial cells. He, therefore, regarded the majority of the peritoneal nodules identical with the so-called pseudomyxoma peritonei. The finding indicates that even in the process of a colloid cancer, all of the peritoneal nodules may not represent true metastases, but many of them are the result of partial organization of masses of colloid which have escaped from the tumor. It must be admitted that colloid cancers have the peculiarity in the remarkable degeneration of their epithelial structures. The author admits that the various stages in the disappearance of the cancer cells may not uncommonly be observed in the secondary growths. When this has occurred upon the peritoneum some care must be taken in distinguishing the cubical cells of the peritoneum under conditions of chronic inflammation from true cancer cells. From the standpoint of diagnosis, these peritoneal tumors offer unusual difficulties. Not a few of them have been described in association with myxoma of the appendix and in their portions of the mucosal epithelium are quite frequently seen. In the absence of a clear history of the origin of the colloid material a positive conclusion as to the nature of such a pseudocyst cannot be arrived at. The author also refers to other types of pseudocysts of the peritoneum. Such may arise through the encapsulation of various foreign materials within the peritoneum. He reports a case of an ovarian dermoid with the development of many calcified cysts in the peritoneum. The case is interesting only insofar as indicating that the peritoneum is very active in encysting foreign materials.

**Leukosarcomatosis and Myeloblastic Leukemia.**—STERNBERG (*Ziegler's Beiträge*, 1915, lxi, 75) desires to separate from the leukemias

particular types of disease which, although showing blood pictures suggestive of leukemia, are nevertheless distinct from these. Under the first group, leukosarcoma, he reports 8 cases, 6 of which showed the pathological characters of lymphosarcoma of the mediastinum and the remaining 2, those of chloroma. They differed, however, from lymphosarcoma in that the blood showed an enormous increase in white cells varying from 100,000 to 800,000. All cases were fatal in less than three years. The tumor tissue resembled the lymphosarcoma on microscopical examination. The spleen was enlarged in all but one. The majority of the white cells of the blood were myeloblasts. The author believes that the masses within the thorax and bone marrow are of lymphatic origin and that the abnormal white cells found in the blood are tumor cells of malignant type. The unusual blood picture with the high count of tumor cells appeared to be a terminal character rather than a feature of the disease. The author, furthermore discusses myeloblastic leukemia. In a series of 21 cases there were 7 men and 14 women, the majority of whom were under middle age. The disease was very acute, accompanied by fever and commonly fatal. Inflammatory conditions about the mouth are frequent and purpura is almost always present. He has found that 7 of the cases examined bacteriologically 5 showed evidence of a bacteremia. These cases showed no great increase in the white-cell count, but myeloblasts were present in high proportion. He believes that these cells appear in the blood as a result of a general infection giving rise to a myelocytosis. These cases are not to be included in the leukemias, some being rapidly fatal, others completely recovering.

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**The Influence of the Roentgen Rays on the Production of Antibodies.**—The influence of the Roentgen rays upon various tissues and their functional activity has elicited much interest particularly in regard to the production of antibodies. In general the tissues most readily affected are the lymphoid group and the bone-marrow. Atrophic changes are quite readily produced in each of these structures and with their destruction the leukocytes are materially diminished in the circulation. The observations that have been made upon the cellular changes associated with exposure to Roentgen rays have a bearing upon studies in immunity. HEKTOEN (*Jour. Infect. Dis.*, 1915, xvii, 415) undertook a series of experiments to determine the effect of the Roentgen rays upon the hemolysins and leukocytes. Rats were used in the experiments. The animals were subjected to the Roentgen rays either before, at, or after the intraperitoneal injection of sheep's corpuscles. The time of exposure varied. Repeated mild exposures after the blood injection reduced the number of leukocytes but did not materially affect the development of lysins. Repeated and more intense exposures preceding as well as succeeding the inoculation had a decided effect in lowering the amount of lysins and reducing the leukocytes. A single prolonged and severe exposure immediately before the injection of blood may prevent any formation of lysin or delay its appearance. As it was found that in all of these experiments the spleen, thymus, lymph glands and bone marrow are the tissues particularly affected by the exposures, it seems reasonable to assume that certain antibodies at least have their origin here. This may also indicate the role of the lymphocyte in tuberculosis in producing antibodies.

**Necrobiosis due to the Electric Current.**—The effect of the electric current upon the function and structure of tissues has been studied by various authors. In many instances the exact nature of the current was not known, while in others, attention was given only to individual regions. Hemorrhage of the central nervous system (Hofmann, Kratter) and alteration of the chromatin substance of the nerve cells (Corrado, Swietalski) have been observed in fatal accidents in man, while somewhat similar results were obtained in experiments by Jellinek in frogs, rabbits, and dogs. Recently BOLOGNESE (*Lo Sperimentale*, 1916, lxi, 869) carried out a series of experiments upon six rabbits using an alternating triphasic street current, and applying the terminals to the flank and the thigh. No record was kept of the strength of the current. The applications were made for periods of thirty to one hundred and twenty seconds. An oval zone about 9 cm. in length was involved by the passage of the current. A certain amount of scorching of the surface was induced while the deeper tissues became rigid and dry. A progressive gangrene developed in the tissues of the involved area and process of degeneration continued for several days during which the animals were under observation. None of the animals were killed by the application of the current. The tissues affected were examined at intervals from three to twenty-four hours after treatment. Important changes were developed in the arteries. Many vessels were found completely thrombosed by red clot. The walls of the femoral arteries showed degenerative changes particularly affecting the elastic tissue. The wall itself appeared thinned and the muscle tissue granular or hyaline. The elastic fibers either appeared broken or swollen and degenerated. The usual wavy character seen in vessels removed from the body, was absent, as if the elastic and contractile power of the arterial wall had been lost. Hemorrhages sometimes appeared about the vasa in the adventitia. Similar changes were present in the veins. The nerves in the involved area showed hyperemia of the small nutrient vessels and occasionally the presence of hemorrhage. Degenerative changes were also seen in the nerves, particularly evident in the presence of granular destruction of the myelin sheaths as well as swelling of the axis cylinders. Cellular changes in the nerve sheaths were not prominent. In the muscle tissues, degeneration with hemorrhage was the most marked feature, while various degrees of necrosis were observed in the muscle fibers themselves. Fragmentation of the muscle substance was also found. The author believed that the effect of the electric current was more far-reaching than is demonstrated by the necrosis, and that the milder degenerations seen in the early stages may progress to the severe conditions after various periods of time.

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ORIGINAL ARTICLES

THE RESPIRATION CALORIMETER IN CLINICAL MEDICINE.\*

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(From the Russell Sage Institute of Pathology in affiliation with the Second  
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IN these days when the housewives speak in terms of calories and the newspapers deal with vitamins it may be well for clinicians to examine once more the fundamental principles of nutrition. Patients no longer demand medicines but they do expect diets, and if they are at all up with the magazine literature, they are better informed on the subject than the text-books which most of us studied in the medical schools. The diets which patients receive in most of our hospitals were laboriously compiled several generations ago and modified from time to time by hospital dietitians. Foods were classified according to their solidity as administered, regardless of what happened in the stomach. Details were left to the head nurse and sometimes to their probationer, and while the patient always had the veto power because he could vomit he was seldom able to initiate legislation.

The science of nutrition in disease must be founded upon experiments in calorimetry and the respiratory metabolism. It may be well at this point to state just what is meant by the term metabolism. The word in itself indicates the transformation of matter and refers to the breaking down of foods, to their absorption, and to the building up of body tissues. The term also refers to the

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oxidation of food-stuffs and of body tissues, with the consequent liberation of warmth and energy. Analysis of food, urine and blood gives an incomplete picture, and it is only through a study of the gaseous exchanges in the tissues that we can study the total metabolism. There are many phrases which have the same meaning as total metabolism. Frequently it is spoken of as *the* metabolism. Sometimes it is called the total energy requirement, total food requirement or heat production, total oxidative processes or total gaseous exchange.

In the years between 1892 and 1908 there was no work being done on this subject in our American hospitals, although Atwater and his successor Benedict, in Middletown were making classical experiments on normal men, and Lusk, here in New York, was making similar experiments on dogs. During this same period in Germany the respiratory metabolism was being studied in a dozen clinics and the investigators were hoping that at some time means would be found to apply the apparatus of Atwater and Benedict to the study of disease, since this alone would solve certain problems. About seven years ago, Benedict and Joslin,<sup>1 2 3</sup> in Boston, began to study the respiratory metabolism of diabetes, and four years ago investigation of the gaseous exchanges of typhoid patients was begun in Bellevue Hospital.<sup>4</sup> Shortly afterward the directors of the Russell Sage Institute of Pathology decided to turn over their funds to Professor Graham Lusk for a period of five years in order that a calorimeter might be built and maintained in Bellevue.

This respiration apparatus is perhaps the most complicated piece of machinery used in modern medicine, but the principles involved in its construction are simple. The description would seem to be a mass of technical details were it not for the fact that it illustrates beautifully the manner in which medicine is founded on physiology and physiology on physics and chemistry.

The first Atwater-Rosa<sup>5</sup> calorimeter in Middletown was a large chamber in which a man could lie in bed, stand up or ride a stationary bicycle. This apparatus is now in Washington, under the charge of Langworthy and Milner<sup>6</sup> who have made many improvements. Atwater's work, however, has been chiefly continued by Dr. F. G. Benedict,<sup>7 8</sup> of the Nutrition Laboratory in Boston, where great advances in the science of calorimetry have been made. Dr. H. B. Williams,<sup>9</sup> of New York, who constructed the small and very accurate calorimeter for Lusk at the Cornell Medical College, has added many ingenious devices. The Sage calorimeter was finished by Mr. J. A. Riche and Mr. G. F. Soderstrom,<sup>10</sup> in the early part of 1913. It has all the modern improvements and is especially adapted for clinical work where observations must be short. Fortunately it is situated in a room near the medical wards of the second division of Bellevue. It is next door to a small diet kitchen

and metabolism ward, where three specially trained nurses weigh out the food and collect the specimens.

The calorimeter itself consists of a copper box about the size of the lower berth of a sleeping car. It contains a comfortable bed and is provided with two windows, a shelf, a telephone, a fan, a light, and a Bowles stethoscope for counting the pulse. The ordinary experiment takes about as long as a trip from New York to New London, and there is an agreeable absence of cinders. Patients, as a rule, doze from time to time or else try to work out some scheme by which they can amuse themselves without moving. After three or four hours they are rather bored by the quiet, and the observations are not prolonged beyond this time. They are allowed to turn over in bed once or twice an hour, but reading and telephoning are discouraged, since these increase the metabolism. The air in the box is fresh and pure, the patient suffers no discomfort, and objections to the procedure are very infrequent. Most of the patients are only too glad of the extra attention, and they insist that the calorimeter has a marked therapeutic value.

The apparatus has two distinct functions: (1) the physical measurement of the heat production of an individual by the method of direct calorimetry; (2) the chemical measurement of his gaseous exchanges and the calculation of the heat by the method of indirect calorimetry. Both depend on the fact that the apparatus is a closed circuit, absolutely shut off from the surrounding atmosphere in such a manner that everything eliminated by the subject is caught and measured.

None of the heat radiated from the man's body can travel through the insulating walls of the calorimeter. All is caught and measured in a stream of cold water flowing through a pipe in the top of the box. It is necessary to measure also the heat dissipated from the body in the vaporization of moisture from skin and lungs. A man loses about one-quarter of the total heat in this manner, and the 20 to 30 grams of water evaporated each hour are caught in a sulphuric acid bottle in the ventilating current. The grams of water multiplied by the factor for the latent heat of vaporization gives us the calories so eliminated. These measurements are very accurate, but it is difficult to determine how much heat a man stores in his body when his temperature rises or how much he releases from his body when his temperature falls. The rectal thermometer does not always tell us of the changes in the average body temperature, and an error of  $0.1^{\circ}$  C. may cause an error of 5 or 6 calories. It is for this reason that direct calorimetry is difficult when the fluctuations of temperature are great. When short periods are employed we therefore place our chief reliance on the method of indirect calorimetry.

This second method is entirely chemical; and, since it involves

a different set of measurements, it serves as an excellent check on the accuracy of the results. The calorimeter is air-tight, and is connected with a series of absorbing bottles by means of a closed circuit or pipes. Air is drawn from the foot of the box by a rotary blower, passed through a bottle of strong sulphuric acid to remove the water vapor and then through weighed bottles of soda-lime and sulphuric acid, which catch the carbon dioxide. By noting the change in weights of these bottles the amounts of water and carbon dioxide removed may be determined. The air thus purified is returned to the box and is used again and again. Meanwhile the subject is consuming oxygen, and this would decrease the volume of gases within the box were it not for the fact that oxygen is automatically admitted from a weighed bomb to compensate exactly for the amount consumed. If we divide the liters of carbon dioxide produced by the liters of oxygen consumed we obtain the respiratory quotient. Knowing this and the amount of nitrogen eliminated in the urine it is possible to calculate the grams of protein, fat, and carbohydrate metabolized each hour. From their well-known heat values we can reckon out the calories produced. With the exception of a portion of the protein molecule each food-stuff is oxidized to the same end-products and with the same liberation of heat in the body as in the Liebig combustion furnace or the bomb calorimeter. The process is slower but just as complete, and there is no loss of energy.

The experimental procedure is not very complicated. A patient is given his ordinary supper in the evening. The next morning his breakfast is withheld and he is put in the calorimeter at about ten o'clock. By eleven o'clock the machine is brought into thermal equilibrium and the experiment is started. At the end of each hour the ventilating current is switched to a new set of absorbing bottles, and by one or two o'clock the observation is over. Calculations consume an hour or so more, and as soon as the urinary nitrogen is determined we have the following information in regard to the patient in hourly periods: consumption of oxygen; output of carbon dioxide; output of water and the total calories; percentage of calories furnished by protein, by fat, by carbohydrate; percentage of heat lost by vaporization, by radiation, and conduction and by storage in or loss from the body; and finally, total metabolism and its relation to the average normal figure, this total metabolism being measured by two independent methods. As may be supposed, these activities keep the three observers fairly busy, since they involve about 40 weighings, 500 temperature readings, and the writing of over 4000 figures.

The accuracy of the calorimeter is tested at regular intervals by burning known amounts of alcohol and comparing the actual findings with the theoretical. In 9 such tests the average error



for heat production was 0.9 per cent., for oxygen 1.2 per cent., for carbon dioxide 0.8 per cent. The total errors are even smaller.

It is hardly necessary to point out that the results obtained with the calorimeter are due to the team work of the whole staff, including the nurses who administer the diets and the chemists who analyze food, blood, urine, etc. Those chiefly responsible for the work here presented are: Dr. Lusk, the scientific director; Mr. Gephart, Dr. Meyer, Mr. Soderstrom, Mr. Harries, Miss Magill, all of the Sage staff, and our associates, Dr. Warren Coleman, Dr. F. M. Allen, and Dr. F. W. Peabody.

There have been many types of apparatus used in the study of the respiratory metabolism in disease.<sup>11</sup> Unfortunately time does not permit of their description, but one cannot help mentioning by name the Pettenkofer-Voit chamber, the Zuntz-Geppert apparatus, the Benedict Unit,<sup>12 13</sup> and the Paschutin calorimeter.

The main object of all investigators has been to determine the heat production of the patient while at complete rest fourteen hours or more after the last meal. This is the so-called basal metabolism, and is of interest only when compared with the figures obtained on normal individuals. Since it is impossible to measure the metabolism of many of our patients when they are entirely recovered, it is necessary to calculate what the man's metabolism would be were he normal. Here lies the most difficult problem. Controversies have raged more fiercely about the normal controls than about the pathological cases. It has been said that a man is as old as his arteries. It may also be said that a piece of research work is as good as its normal controls.

The normal controls used by investigators up to the last few years often showed a variation of 50 per cent. above or below the average. It was discouraging to run the calorimeter within an error of 1 or 2 per cent. and then compare the results with such an uncertain figure. Now this variation in the normals was largely due to the manner in which the results were expressed. If we leave the calculations, as was previously done, in the stage of cubic centimeters of carbon dioxide per kilogram of body weight there might be a large apparent variation between two men whose heat production is identical. Part of this error is eliminated if we express the results in calories, and still more eliminated if we base our calculations on surface area rather than body weight. A large man, of course, gives off more heat than a small man, but for each kilogram of body weight the small man has the higher metabolism. Rubner<sup>14</sup> demonstrated many years ago that the metabolism is proportional to the surface area of the body and that for each square meter of skin large men, small men, dogs, horses, and mice have about the same heat production. Just why this should be we do not know. It reminds us at once of Newton's law that the cooling of bodies

is proportional to their surface area, but the metabolism does not follow this law when the external temperature is raised or lowered.

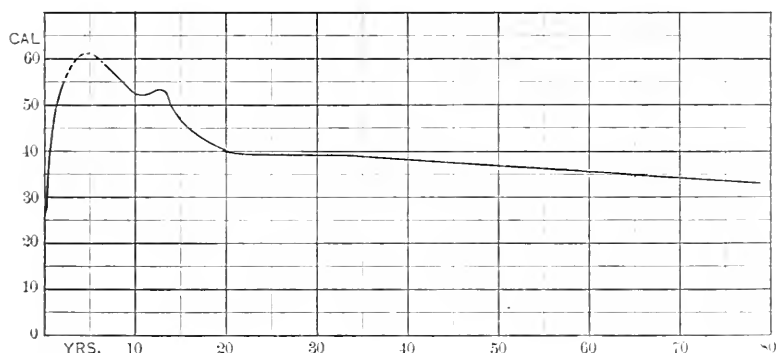
There are several formulas which allow us to calculate the surface area of a man. Meeh's<sup>15</sup> formula, which is proportional to the two-third power of the weight has been the standard for over a generation, and up to the last year entered into almost all the calculations. One divided the calories produced per hour by the square meters of surface area and obtained the calories per square meter per hour. Very recently the accuracy of Meeh's formula was investigated by the Sage staff. Mr. Delafield Du Bois<sup>16</sup> devised a method of measuring the skin area which has been applied to ten individuals of every conceivable shape. He found an average plus error of 16 per cent. in Meeh's formula and an error of 36 per cent. in fat subjects. To correct these the so-called "linear formula" was devised and also a simpler formula based on height and weight.<sup>17</sup>

It is interesting to group the normal controls studied in the Sage calorimeter<sup>18</sup> with the large number of healthy men and women studied by Benedict, Emmes, Roth and Smith in Boston,<sup>19 20 21 22 23</sup> and also by Palmer, Means, and Gamble.<sup>25</sup> If we plot the men under fifty years of age according to calories per square meter of surface area we find that all are within 15 per cent. of the averages and 86 per cent. are within 10 per cent. of the average. According to Meeh's formula thin people have an increased metabolism and fat people a very low metabolism. Using the more accurate linear formula, Means<sup>24 25 26</sup> has found the metabolism in most cases of obesity to be within normal limits, and if we recalculate the figures for groups of thin men and fat men according to their true surface area the results in the two groups are almost identical.

We can therefore feel certain that with men between the ages of twenty and fifty the metabolism of each individual is proportional to his surface area whether he be short or tall, fat or thin. We can compare all our pathological cases with the normal average basal metabolism of 31.7 calories per hour per square meter of surface according to Meeh's formula, or, better still, 39.7 per square meter according to the new so-called linear formula. The normal variation from this average is plus or minus 10 per cent. and a few apparently normal men show a variation of 15 per cent. We cannot consider the metabolism of an individual patient to be abnormal if within these limits, but if a group of patients gives an average of more than 10 per cent. from the normal base line we can feel certain that there is a pathological change in the heat production in that particular disease.

Comparisons of different persons can be made only by determining the basal metabolism. There are many factors which cause certain groups of normal individuals to depart materially from our

mean figure of 39.7 calories per square meter per hour. Women give an average about 6 per cent. below this,<sup>22</sup> athletes are about the same distance above, as has been shown by Benedict and Smith.<sup>21</sup> Age causes a marked difference which will be discussed later. The metabolism seems to be higher in the afternoon than in the morning, and during profound sleep there is a drop of 5 to 20 per cent. The metabolism is 5 to 10 per cent. higher sitting upright in a chair than when lying down, but it has recently been found that the metabolism of subjects propped up comfortably in a steamer chair is a little lower than when they are lying flat in bed.<sup>27</sup> This throws some light on one of the many causes of the assumption of the orthopneic position by patients. It lends scientific support to the empirical observation that a lazy man is happiest with his chair tilted back and his feet on the desk.



Variation of basal metabolism with age. The curve shows the changes in the level of the heat production from birth to old age. The results are expressed in terms of calories per square meter of body surface per hour. Only male subjects were used in making the curve. The surface area was estimated by the linear formula or the comparable height-weight formula except in the case of the infants, where it was necessary to use Lissauer's formula. The normal variation from the above line is plus or minus 10 per cent. Details of this curve will be published in the Archives of Internal Medicine.

As I have said, the basal metabolism is measured fourteen hours or more after the last meal because food stimulates the metabolism. This is due to the so-called specific dynamic action of foods, and is greatest in the case of protein and least in the case of carbohydrate. The phenomena, first discovered by Rubner,<sup>28</sup> have been studied in great detail by Lusk,<sup>29</sup> using the dog calorimeter at the Cornell Medical College. He has found that the specific dynamic action of protein is due to the stimulus of the metabolism products of amino-acids acting upon cell protoplasm, and that although the preliminary cleavage products of fat and carbohydrate do not appear to be direct stimuli, yet when they are present in excess in the fluid bathing the cells, the heat production is increased. With the normal controls in the Sage calorimeter<sup>18</sup> a standard

protein meal containing 10 grams of nitrogen causes an average increase of 12 per cent. in the five to six hours after its ingestion, and 100 grams of dextrose causes an increase of 9 per cent. These same meals have been used to test the specific dynamic action of foods in typhoid fever and exophthalmic goitre.

The curve showing the effect of age on heat production is of special interest. Magnus-Levy and Falk<sup>30</sup> demonstrated that the metabolism was high in childhood and low in old age, and no one will doubt this who has compared the amounts of food consumed by children and by their grandparents. We have now at our command a large number of observations made at all ages except the period between the second and sixth years. The reason for this gap is apparent. The shortest experimental period is ten minutes, and normal children of this age are never quiet for this length of time. The metabolism of infants has been studied by Howland,<sup>31</sup> Benedict and Talbot,<sup>32 33 34</sup> by Murlin and Hoobler,<sup>35</sup> Bailey and Murlin<sup>36</sup> and others. Eight boy scouts, not long ago, were studied in the Sage calorimeter<sup>37</sup> and made to keep quiet by a system of fines and rewards. If we tabulate these with all the other children and adults we can trace a curve which shows the heat production per square meter of surface at different ages, and compare it with the average adult figure. During the first few weeks of life the metabolism is very low, after which it rises rapidly until at the end of the first year it is 50 per cent. above the adult level. The curve reaches its acme in the almost unexplored period between two and six years and then falls fairly rapidly until the age of twenty years. After this the decrease is extremely gradual.

Just why newborn infants should have such a low metabolism we do not know. It is conceivable that the high metabolism of older children is in part due to the relatively large size of the head, body, and especially the liver. Men with their legs cut off resemble babies in the relative proportions of body and extremities. Two such individuals studied in the calorimeter have been found to have a high metabolism. This would not explain the high metabolism of the boy scouts who have reached the adult proportions although they have not attained adult size. Theorists might go so far as to say that the increased heat production proves in itself an increased thyroid activity in childhood. It is safer for several reasons to ascribe it to some unknown stimulus associated with growth. For the level of metabolism falls as the rate of growth decreases, but rises again in the case of the boy scouts just before the onset of puberty, a period when the rate of growth is once more accelerated. Again, in adult life the nearest approach to the growth of childhood is found in convalescence from acute infectious diseases, and there is a distinct rise in metabolism in the convalescence from typhoid fever.<sup>4 38</sup>

**METABOLISM IN DISEASE.** The most striking disease from the standpoint of changes in the total metabolism is exophthalmic goitre, and clinicians who pay no attention to the gaseous exchanges neglect the most important phase of this malady. Friedrich Müller first called attention to the high metabolism in Basedow's disease by noting the nitrogen and weight losses of patients taking enough food to maintain normal subjects in nutritive equilibrium. Magnus-Levy<sup>40 41</sup> found the gaseous exchanges very high in Graves's disease and very low in myxedema.<sup>42</sup> His results have been amply confirmed by Stüve,<sup>43</sup> Hirschlaff,<sup>44</sup> Salomon<sup>45</sup> and others, and by those of us working with the Sage calorimeter.<sup>46</sup> If we group 33 cases of hyperthyroidism studied by other investigators with the 11 studied in New York, we find that the increase in metabolism is strictly proportional to the severity of the clinical symptoms. One fatal case of Hirschlaff's in the last two weeks of life showed an increase of 120 per cent. above the average normal and two severe but non-fatal cases at Bellevue have given results which are 100 per cent. above the normal. In general, it may be said that very severe cases show an increase of 75 per cent. or more, severe cases 50 per cent. or more, moderately severe and mild cases less than 50 per cent., while a few mild, atypical or operated cases may be within normal limits.

This increase in metabolism is the most striking effect of thyroid activity, and it is equalled in no other disease. In cretinism and myxedema the metabolism may be 25 to 50 per cent. below the normal level. Thyroid extract raises the metabolism in these conditions and has a similar though less constant effect on normal men and obesity patients. No other glandular extract yet examined has this property in any significant degree. Many of the symptoms of hyperthyroidism are secondary to the abnormal heat production. The flushed, warm skin and the sweating are physiological methods of dissipating extra heat. The increased appetite and the loss of weight that sometimes occur in spite of this are the results of increased calorific requirements. Part of the tachycardia is certainly due to the greater demands for oxygen.

Most of the investigators who have studied the gaseous exchanges in this disease have used the level of the metabolism as an index of the effect of treatment. This procedure is perfectly logical, and it is particularly desirable to have some purely objective guide to therapeutics in a disease where there is so much psychotherapy on the part of the physician and patient. Previous observers have found no change in the metabolism after the administration of rhadogen,<sup>45</sup> Roentgen rays,<sup>47</sup> and the serum of thyroidectomized animals,<sup>48</sup> but have established a prompt drop after partial thyroidectomy.<sup>48</sup> In the cases observed at Bellevue a fall of 10 or 15 per cent. has resulted from rest alone, and none of the other therapeutic measures tried gave any better results. These included

Beebe's serum, ergotin, and quinin hydrobromate, and finally thyroid residue. But since the two former methods were tried on only one patient it is not fair to condemn them. With several patients the thyroid arteries were ligated, and it was found that this procedure caused a sharp rise in the metabolism which fell subsequently to its former level. The operative procedure, although very conservatively done under local anesthesia, increases temporarily the activity of the gland. There is as yet no proof that any form of medical treatment or ligation of arteries causes a greater reduction in metabolism than rest in bed. Several important facts have been brought out in regard to the administration of food to Basedow patients. They need large amounts of food with an abundant, though not excessive, protein ration. Von Noorden<sup>49</sup> has warned us against the use of large amounts of protein and especially meat, assuming that it causes a greater rise in heat production in sickness than in health. Pribram and Porges<sup>47</sup> found that after a diet with large amounts of meat the metabolism was slightly increased, but not more so than in normal people. Undenisch<sup>48</sup> found that the protein of meat causes less stimulation than vegetable proteins. With the Sage calorimeter it has been found that the specific dynamic action of protein and carbohydrate with exophthalmic goitre patients is not appreciably different from the normal, and that there is no significant difference between the effects of meat and the same amount of protein in milk and eggs. It has taken a large amount of work to disprove the hypothesis of a prominent specialist. Still, it is a great relief to know that we need not worry our patients with restrictions on the kinds of proteins they take. The protein ration should contain about 12 to 15 grams of nitrogen a day, which is the amount ordinarily consumed.

The carbohydrates are readily metabolized in spite of the moderate glycosuria found in severe cases. Except in the true cases of diabetes with goitre it is an abnormality of mobilization rather than utilization. One of the severe cases at Bellevue Hospital was able to derive 90 per cent. of his calories from the oxidation of carbohydrates in spite of a marked glycosuria. A severe case of diabetes could not have derived 10 per cent. of his calories from this source, and even a mild case would scarcely have reached the figure of 50 per cent. Goitre patients use up carbohydrates rapidly, and fourteen hours after their last meal are maintaining themselves almost entirely on fat and protein.

In regard to the medical treatment of Graves's disease the calorimeter may be a therapeutic Nihilist, but it is a dietetic enthusiast, and it is also a strong supporter of the belief that mental and physical rest are essential in the treatment of severe cases.

DIABETES MELLITUS. The Harvey Society is fortunate in having, almost every year, a lecture devoted exclusively to the fascinating

subject of diabetes mellitus. The respiratory metabolism was discussed last year in a masterly fashion by Joslin,<sup>50</sup> who, with Benedict, in Boston,<sup>1 2 3</sup> has done an enormous amount of work on this subject. During the past year, working in coöperation with Dr. Allen,<sup>51</sup> of the Rockefeller Hospital, it has been possible to study in the greatest detail one particularly severe case of diabetes snatched from coma by the Allen fasting treatment. This case and several others also studied have given such striking confirmation to the views held by Lusk,<sup>52 53 54 55</sup> for many years, that it is impossible to pass the subject by. Lusk was the first to maintain that a patient who was completely diabetic would excrete not only all the ingested carbohydrate but would also turn about half of the protein molecule into sugar and excrete it in the urine. Under these conditions the excess of excreted sugar over ingested would be about three and a half times the nitrogen in the urine: in other words, the D : N ration would be 3.65. Under these circumstances the respiratory quotient would be depressed below that of fat by the incomplete combustion of protein instead of being raised by protein as with normal people. The lowest possible quotient in health is 0.72, and in complete diabetes with the D : N ratio 3.65, Lusk has calculated that the quotient might be depressed to 0.69. One of the severe cases above mentioned with the D : N of 3.5 showed a quotient of 0.697, another with the D : N of 3.1 gave a quotient of 0.692. There was absolutely no evidence of any formation of sugar from fat. The D : N ratio if determined under the proper precautions is certainly the best guide as to the severity of the case.

The effect of the Allen<sup>56</sup> fasting treatment in the severe case most completely studied was to cause a gradual rise in the quotient as the D : N ratio fell and the glycosuria cleared up. After the fast the curious phenomenon mentioned by Joslin<sup>50</sup> was noted. There was a rise in quotient indicating the combustion of carbohydrate from some unknown source. This may be stored glycogen, excess of sugar in blood and tissues, or perhaps it may be due to the oxidation of acetone bodies.

Another effect of the fast was the marked fall in total metabolism. The patient was brought to a condition where his low food requirement could be met by his improved though still damaged metabolic functions. The metabolism was reduced to a point even lower than that reached by normal men fasting a long time.

This brings us to the question of the total metabolism in diabetes, still the subject of controversy. The older investigations by Pettenkofer and Voit,<sup>57</sup> Nehring and Schmoll,<sup>58</sup> Magnus-Levy,<sup>59</sup> Du Bois and Veeder<sup>60</sup> and others indicated only a slight increase in total metabolism. More recently Benedict and Joslin,<sup>1 2 3</sup> who have studied a large number of cases, have maintained that the metabolism averages about 15 per cent. above the normal in severe

diabetes, and Rolly<sup>61</sup> and Leimdörfer<sup>62</sup> reached the same conclusion. Lusk<sup>63</sup> has gone over the results obtained by Benedict and Joslin using different normal controls for the purposes of comparison, and has concluded that the metabolism is but slightly increased. An interesting light has been thrown on this subject by the new method of calculating the surface area. It was noted in one severe case of diabetes, studied before the fast at Bellevue Hospital, that the metabolism was 2 per cent. above the average figure according to Meeh's formula, but 8 per cent. below according to the true surface area. Patients with severe diabetes are usually very thin, and in such cases comparisons based on Meeh's formula are untrustworthy. If we recalculate the severe cases of Benedict and Joslin by means of the new height-weight formula we find that the average is about 3 per cent. above the standard figure of 39.7 calories per square meter per hour. The cases studied at Bellevue were all below the normal, but some of them were low on account of fasting. (One patient very recently studied showed a slight increase in metabolism for a few days. His acidosis and also his nitrogen elimination were unusually high.)

**TYPHOID FEVER.** Typhoid lends itself particularly well to a study of the changes in metabolism which occur in fever. It is more uniform in its course than most fevers, is protracted, is often severe, and is with us every autumn. There are several factors at work in a typhoid patient: (1) toxemia, (2) fever, and (3) more or less starvation. Since the introduction of the Shaffer-Coleman<sup>65</sup> high calory diet this last factor has almost disappeared, leaving a much more satisfactory disease for the patient and for the scientific investigator. The work done on the nitrogen metabolism has been voluminous, and the controversy concerning the toxic destruction of protein is still violent. The respiratory metabolism has been studied by many investigators, notably Kraus,<sup>66</sup> Svenson,<sup>67</sup> Grafe,<sup>68</sup> and Rolly.<sup>69</sup> At Bellevue Hospital 134 observations with the small Benedict apparatus have been made by Coleman and the writer and 61 with the Sage calorimeter.

The total metabolism in typhoid fever shows an increase which is roughly proportional to the rise in temperature. At the height of the fever it averages about 40 per cent. above the normal, but in some cases may be more than 50 per cent. above. Patients who are liberally nourished with the high calory diet of Coleman and Shaffer do not have a greater heat production than patients on low diets. The Sage calorimeter has shown that the specific dynamic action of protein and glucose is much smaller than normal, and in fact almost absent in typhoid fever. The practical application of all this is that typhoid patients need more food than normal men under similar conditions, and that food even in large amounts is well absorbed and does not increase the heat production, as was previously feared. Typhoid patients like all others with high



metabolism use up their carbohydrate food and glycogen stores rapidly, and this type of food should be given in large amounts if we do not want the patients to subsist on protein and fat obtained chiefly from their own tissues.

The actual heat production of most of the typhoid patients is between 2000 and 3000 calories a day. Such amounts, as a rule, can be readily administered, and to me personally it hardly seems necessary to give more than 3000 calories a day unless the patient wants it. Dr. Coleman, whose experience is much greater than mine, believes that patients do best on larger amounts, since these alone will prevent the loss of body protein.

A series of careful experiments has been made in which the nitrogen and respiratory metabolism was studied at the same time. Now a normal man can be maintained in nitrogen and weight equilibrium if given a moderate amount of protein and enough calories to cover the heat production as calculated from the basal metabolism, with allowance for food stimulation and muscular activity. It has been possible by means of the Sage calorimeter to determine the actual heat production of a series of typhoid patients. In the adjoining metabolism ward the head nurse, Miss Magill, and her assistants have skilfully administered food in sufficient amount amply to cover the caloric output. Yet the patients have shown distinctly negative nitrogen balances during the febrile period, and in one case for several days after the fever had ended. This is conclusive proof that there is an abnormal destruction of protein in typhoid fever, and the evidence indicates that this is due chiefly to the toxins of the disease. Shaffer and Coleman were able to demonstrate that this toxic destruction could be prevented or masked by the administration of very large amounts of food, particularly carbohydrates. Kocher<sup>70</sup> has recently shown that in fever even with large amounts of food the nitrogen excretion can never be reduced to the low point of 3 to 4 grams a day readily obtained in health.

In the early days of convalescence from typhoid the metabolism is slightly below the normal, then it rises to 15 to 20 per cent. above, apparently as the result of the large amounts of food and the stimulus of growth. In convalescence the specific dynamic action of food is either normal or else greater than normal. We do not care if the heat production at this period be increased and there is no contra-indication from the metabolic standpoint to liberal feeding in convalescence.

The problem of the mechanism of the rise and fall in body temperature in fever has been the subject of much experimentation, and the question can be settled only by a respiration calorimeter. For reasons that cannot be discussed in a short paper the technic is difficult, and there are only 11 of the calorimeter experiments in typhoid which meet the rigid requirements. These indicate

that a rising temperature is accompanied by an increasing heat production which outweighs a slightly increasing heat elimination. With a falling temperature the production remains fairly level while the elimination is increased.

**ANEMIAS.** The question of the oxidative processes in cases of severe anemia is of particular interest. When the hemoglobin content of the blood is greatly reduced it is difficult to see how the tissues can be supplied with enough oxygen, and yet every clinician has seen patients with 20 to 30 per cent. of the normal percentage of hemoglobin who are not dyspneic. How is this possible? The blood volume is not increased enough to account for the compensation, the plasma can carry only small amounts of oxygen, the hemoglobin in anemia does not possess an abnormal power to combine with extra amounts of oxygen. Some experimenters have believed that the oxygen requirement in such patients was lower than normal.

The respiratory metabolism in various types of anemia has been studied by Magnus-Levy,<sup>71</sup> Kraus,<sup>72</sup> Bohland,<sup>73</sup> Thiele and Nehring,<sup>74</sup> Grafe,<sup>75</sup> and six cases of pernicious anemia have been observed in the Sage calorimeter by Meyer and the writer.<sup>76</sup> In few cases examined by investigators I have named was the metabolism below normal. In lymphatic leukemia it was often 50 per cent. above normal, perhaps on account of the abnormal oxidative activity of the white blood cells, perhaps on account of lactic acid formation. In two severe cases of pernicious anemia at Bellevue Hospital with 20 per cent. hemoglobin the metabolism was 24 and 39 per cent. above normal.

The chief compensatory factor in such patients would seem to be an increased cardiac output per minute. It appears also that the blood is more completely robbed of its oxygen in its passage through the capillaries.

**CARDIORENAL DISEASE.** The previous works on the gaseous exchanges in cardiac and renal disease have not been extensive and have been marred by respiratory quotients which are so low that it has been necessary for the investigators to assume abnormal processes. Peabody, Meyer and Du Bois<sup>77</sup> have studied 16 patients in the calorimeter, a number which is somewhat small when we consider the variations present in these diseases. In general it may be said that mild cases of nephritis and compensated cardiac patients are within normal limits, as are a few severe cases of both diseases. An increase in heat production amounting to 30 to 40 per cent. is found in most of the very dyspneic patients. The cause of the rise may be in part the increased work of respiration and increased labor of the heart, but the chief factors are yet to be discovered.

There is no evidence of profound changes in the intermediary metabolism in cardiac and nephritic dyspnea. Not a single ab-

normal quotient has been found by the calorimeter. We must remember that the patients with high metabolism use up more food than normal men, and with ordinary diet will suffer from partial starvation. If not given large amounts of carbohydrate in the food they will subsist chiefly on fat and protein derived largely from their own tissues. It is worth while to remember these things when we order the restricted diets which seem necessary in many cases of cardiac and renal disease.

**MISCELLANEOUS CONDITIONS.** Many other diseases have been studied in various clinics, but it is impossible to discuss them at length. Grafe<sup>78</sup> has found an increase in metabolism in cancer and only a moderate increase in low-grade fevers. Various diseases of the pituitary have been studied by Falta<sup>64</sup> in Vienna, by Means<sup>24</sup> in Boston, and by the Sage staff in Bellevue Hospital.<sup>79</sup> Results are variable and no conclusions can be drawn as to any marked change in the respiratory metabolism except that in acromegaly there is slight but fairly constant rise in heat production. The metabolism of women just before and just after childbirth was studied most carefully by Carpenter and Murlin<sup>80</sup> using one of the calorimeters in Benedict's laboratory. The effect of drugs on the heat production of men has been studied by Loewy,<sup>81</sup> Lindhard<sup>82</sup> and others and important work is now being done on this subject by Edsall<sup>83</sup> and Higgins and Means.<sup>84</sup>

We must not forget that much of our knowledge of the respiratory metabolism in disease is due to the work done on animals and normal men. We need only mention the researches in this country of Lusk, Benedict, Murlin, Carpenter and many others.

**GENERAL CONSIDERATIONS.** We have seen that the respiration calorimeter measures the heat production by the independent methods of direct and indirect calorimetry. The direct method must remain the standard in the long run and any significant and consistent divergence of the indirect method in any particular disease would indicate a marked change in the intermediary metabolism. It would show that the food-stuffs were not broken down to the same end-products with the same liberation of heat as in normal subjects. Such changes in disease have often been considered very seriously, particularly by investigators who, on account of defective technic, have obtained abnormally low quotients. The calorimeter has obtained no such quotients except in severe diabetes, where they are to be expected. The direct and indirect calorimetry have agreed very closely when we consider the technical difficulties in short observations with sick patients. Until a very few years ago no one would have dreamed of trying to make the two methods agree in periods shorter than six hours. At that time the calculations were not even carried out, but if we now go over some of the work in Benedict's laboratory<sup>80</sup> as early as 1911 we find excellent agreement in two-hour subdivisions of four-hour experiments. With the

Cornell calorimeter built by Williams,<sup>9</sup> Lusk has been able to obtain remarkable agreement in periods as short as an hour with dogs and a dwarf. Howland<sup>31</sup> has obtained similar results with babies. When the totals obtained on all the normal controls studied in the Sage calorimeter are compared it is found that the two methods agree within 0.2 of 1 per cent. With the experiments two to three hours long, such as are used with patients, certain technical errors have a tendency to make the direct calorimetry too low, and we find it 2.2 per cent. lower in typhoid fever, 2.8 per cent. in exophthalmic goitre, 2.3 per cent. in diabetes, 3.3 per cent. in anemia, 1.9 per cent. in the group of cardiac and nephritis patients. These divergences are within the limits of technical error; they are so small that we can be certain that the law of conservation of energy holds good in disease and can also be sure that there are no profound and unsuspected changes in the intermediary metabolism. It is not possible to rule out small changes which might be concealed by the limits of technical error. The chief function of the calorimeter has been to show that the principles of indirect calorimetry are correct when applied to disease. Another function is to make it difficult for overenthusiastic theorists to promulgate wild hypotheses.

The results of work with calorimeters and other types of respiration apparatus must build the foundations of our theories of the nutrition of patients. If we desire to administer to any given patient his exact requirement it is necessary to make several experiments on the patient himself. It is very doubtful if the most experienced observer can guess the heat production of a sick man within 20 per cent. Still, it is possible to make rough calculations which will allow the physician to reckon out the caloric requirements of his patients somewhat more exactly than the trained nurse. We can use as a standard the basal requirement of healthy men between the ages of twenty and fifty and add 10 per cent. for the stimulation of food and about 10 per cent. for the usual activity of a patient confined to bed. Under these conditions the food requirement for the day would be 1800 calories for a man of 125 pounds, 2000 calories for 150 pounds, and 2200 calories for a man of 175 pounds. Bearing in mind the numerous factors already discussed we can add the various percentages according to the disease and its severity. If the patients are permitted to get out of bed, or if they are very restless, we must allow for an increase of anywhere between 20 and 100 per cent. during the hours when they are moving about.

Some observers have attempted to determine the total food requirement in disease by observing the intake and output of nitrogen. Such experiments in nitrogen equilibrium must be continued for weeks to give much evidence on this point. The work at Bellevue Hospital in typhoid fever<sup>38</sup> has shown that a negative

nitrogen balance may exist when the caloric needs are more than covered by the food.

In many cases the fluctuations of body weight serve as a guide to the nutritive condition of the body. We must not place too much reliance on short observations. Rapid changes in weight are due in great part to changes in the water content of the body. Benedict<sup>2</sup> quotes the case of a football player who lost 14 pounds in a game one hour and ten minutes long. Only one-quarter pound was due to the oxidation of solids,  $13\frac{3}{4}$  pounds was water loss. We are familiar with the retention of large amounts of water in edema and are familiar with the role of salts, but we do not realize the frequency of invisible edema. A diet rich in carbohydrates causes the body to retain considerable amounts of water; a fat diet has the opposite effect.

Many clinicians are in the habit of measuring the fluid intake and urinary output under the impression that they are determining the water balance. Patients in the calorimeter eliminate water through skin and lungs at a rate which varies between  $\frac{1}{2}$  and 1 liter a day. The fluids of the diet form but a small part of the water intake. Rennet, a solid food, contains just as much water as milk. Potatoes are 75 per cent. water, tomatoes 94 per cent. An accurate water balance is one of the most difficult problems in experimental metabolism and we must not place too much reliance on changes in weight unless followed for long periods.

In reviewing the subject of metabolism in disease one can see that clinicians too long contented themselves with urinalyses and measurements of intake and output. Now they are thinking in terms of the blood and the fluids which bathe the cells. It is certainly worth while to go one step farther and study more closely the respiratory metabolism which tells of the results of the activities in the tissues themselves.

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## A NEW CLASSIFICATION OF NEOPLASMS AND ITS CLINICAL VALUE.<sup>1</sup>

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I TAKE the liberty of presenting a new classification of neoplasms<sup>2</sup> for the following reasons:

1. It has been clearly demonstrated that carcinoma in three different organs arises from the regenerative cells of the parenchyma of the organs and not from the parenchyma of these organs (breast, skin and prostate).<sup>3</sup>

2. It has been definitely established that cancer cells of different organs of different germinal layer origin are often morphologically indistinguishable.<sup>4</sup>

3. It has been definitely shown that even the best pathologists cannot always differentiate carcinoma from sarcoma, the cells being often morphologically indistinguishable.

4. It may be seen from the writings of many authorities who classify tumors that their classifications are based on the histogenesis of tissues, and that many of these authorities express dissatisfaction with this basis of classification and apologetically accept it as the best, under the existing state of our knowledge.<sup>5</sup>

<sup>1</sup> Read before the Section on Pathology and Physiology of the Sixty-sixth Annual Session of the American Medical Association, San Francisco, June, 1915.

<sup>2</sup> This brief statement of a biological conception of neoplastic cytological processes serves merely as a preliminary report and is presented at the present time for the purpose of stimulating pathologists and clinicians to study their early neoplasms and chronic inflammatory conditions in the light of the process of tissue regeneration. It also serves to point the way to the standardization of histological and cytological facts with clinical experience.

<sup>3</sup> MacCarty, W. C., *Carcinoma of the Breast*, *Old Dominion Jour. Med. and Surg.*, 1911, xii, 189, and *Tr. South. Surg. Assn.*, 1910, xxiii. *The Histogenesis of Cancer of the Breast*, *Surg., Gynec. and Obst.*, 1913, xvii, 111. *Clinical Suggestions Based upon a Study of Primary, Secondary (Carcinoma?), and Tertiary (Carcinoma) Epithelial Hyperplasia in the Breast*, *Surg., Gynec. and Obst.*, 1914, xviii, 281. *The Biological Position of the Carcinoma Cell*, *Collected Papers of the Mayo Clinic*, 1914, vi, 594. *Precancerous Conditions*, *Jour. Iowa State Med. Soc.*, 1914, iv, 1.

<sup>4</sup> MacCarty, W. C., *Notes on the Irregularity and Similarity of Cancer Cells*, *Collected Papers of the Mayo Clinic*, 1914, vi, 600.

<sup>5</sup> Adams, J. G., *Principles of Pathology*, Philadelphia, Lea & Febiger, 1909, i. Borst, M., *Die Lehre von den Geschwülsten*, Wiesbaden, Bergmann, 1902. Councilman, W. T.,

5. A review of embryological facts relative to the histogenesis of the different tissues of the body clearly reveals a lack of definite information relative to the exact origin of many tissues, a fact which places any classification which is founded on the histogenesis of tissues on a theoretical basis.<sup>6</sup>

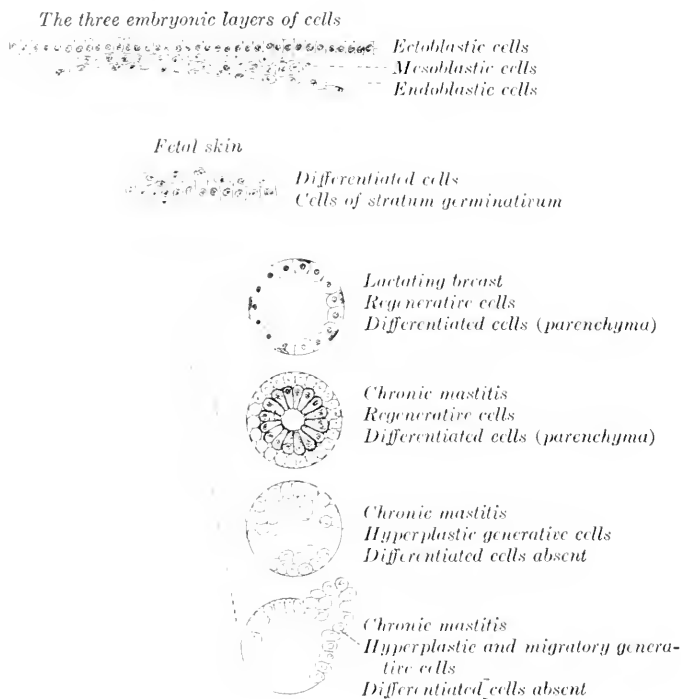


FIG. 1. Diagrammatically shows the embryonic origin of the cells which comprise the mammary acinus and their activity under the influence of the chronic stimulus or stimuli in chronic mastitis and mammary carcinoma.

6. The histogenetic basis for a classification of tumors is also based on the theory of specificity of tissues which finds some contradiction in biological experimental facts and in certain embryological developmental facts.<sup>7</sup>

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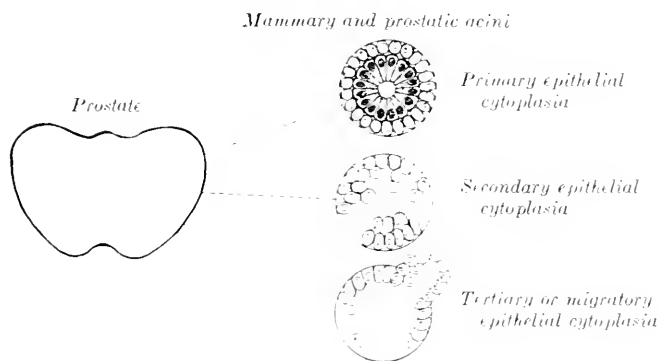


FIG. 2.—The prostatic epithelium presents the same arrangement of cells with the same biological characteristics which are found in the breast.

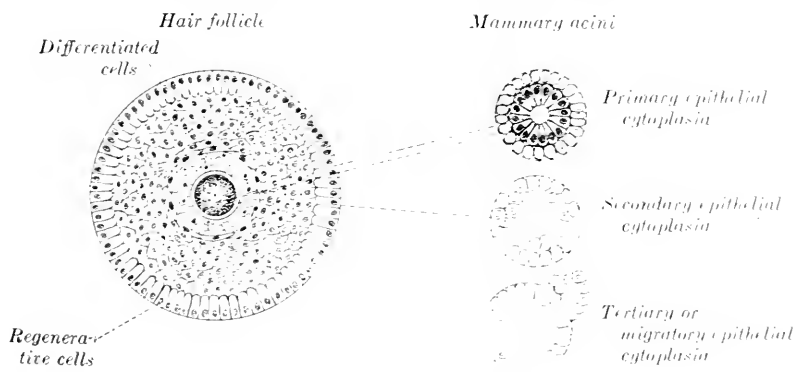


FIG. 3.—The principal cytological changes which occur in the hair follicle in chronic folliculitis are seen in the germinal cells which present the same characteristics which are seen in the mammary acini when undergoing a condition of epithelial hyperplasia.

*Mammary acini*

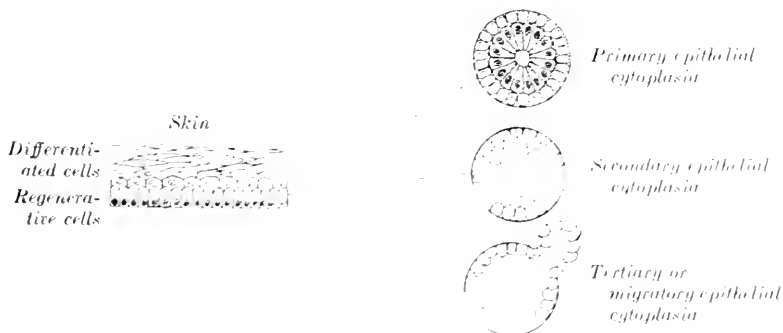


FIG. 4.—In conditions of chronic dermatitis one finds the most marked cytological activity in the germinal layer of cells which present the same characteristics, which are seen in the secondary and tertiary epithelial hyperplasia in the acini of the mammary gland.

7. The classifications which are utilized today by the best authorities do not describe the condition of the cells of tumors but merely name the tumors from the tissues from which they are supposed to, but probably do not, arise.

The classification herewith presented is based on the following established biological facts:

1. The cell is the recognized unit of life.
2. Tissues are communisms of specific or differentiated cells.
3. Organs are communisms of tissues.
4. The fertilized ovum by a process of segmentation produces cells which produce cells, which become differentiated into tissues.

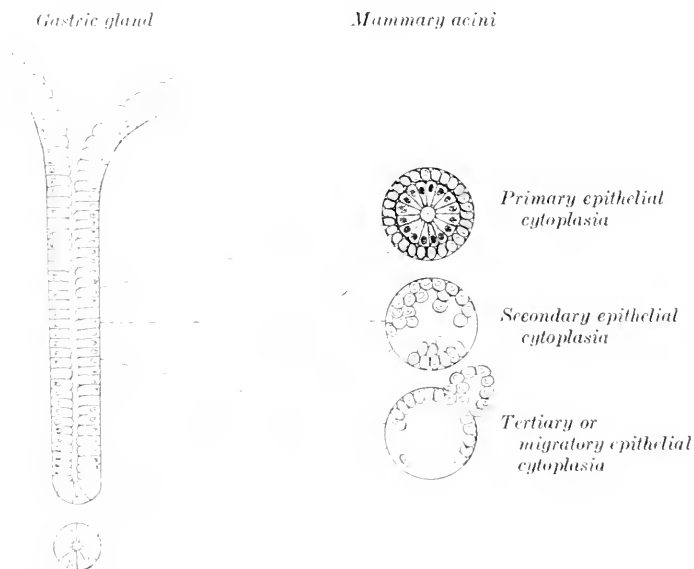


FIG. 5. The analogy between the observations of epithelial hyperplasia in the breast and those in the stomach. The location of the germinal cells in the gastric gland is at present uncertain. In the gastric gland two rows of cells are not seen as in the prostate, breast, skin and hair follicle. However, where the differentiated columnar or cuboidal gastric epithelial cells are normally present, one sees, in chronic inflammatory conditions, certain cytological pictures, which are analogous to those which are seen in secondary and tertiary epithelial hyperplasia in the breast.

5. During the process of the production of cells which produce tissues, certain cells remain in a stage of reserve (regenerative cells) for the purpose of producing specific tissues when the specific tissues are destroyed.

6. In the presence of chronic irritation, specific cells of tissues are destroyed, the reserve cells become hyperplastic, and sometimes in the presence of failure to reproduce specific cells they form an overgrowth, the cells of which sometimes migrate into the stroma.

7. The cytological process of attempted regeneration expresses itself histologically in three definite stages or conditions: (a) by the presence of the atrophic or degenerating specific or differentiated cells plus hypertrophic regenerative cells (primary cytoplasia); (b) by the absence of specific cells plus the presence of hypertrophic and hyperplastic regenerative cells (secondary cytoplasia); and (c) by the absence of specific cells plus the presence of hyperplastic regenerative cells plus migration of the hyperplastic regenerative cells into the stroma, lymphatics, neighboring and distant organs (tertiary or migratory cytoplasia). (See Figs. 1 to 7.)

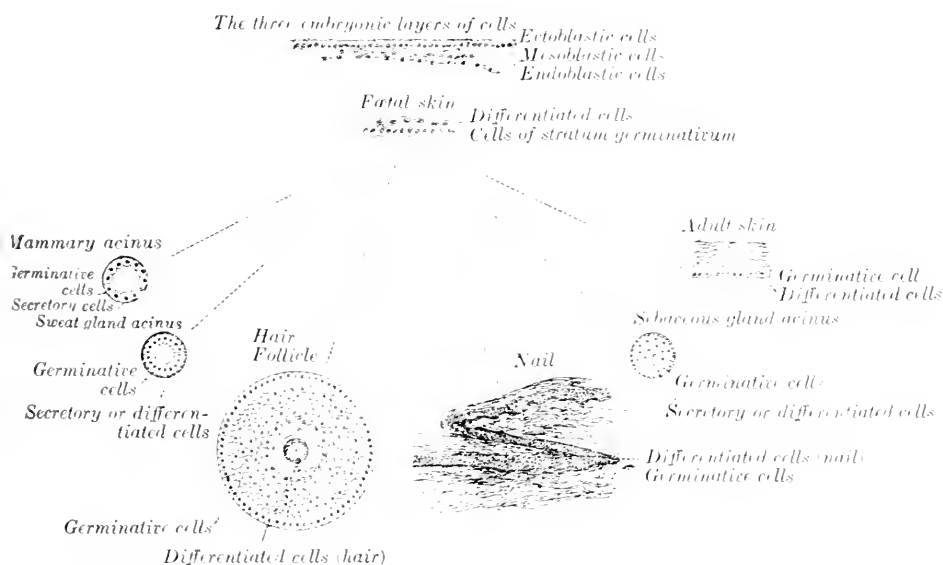


FIG. 6.—Organic differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat glands, sebaceous glands, hair, nails and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin and the epidermis of the skin.

8. The first cytoplasia (primary cytoplasia) represents a condition which is commonly accepted as a clinically benign condition. The third cytoplasia (tertiary or migratory cytoplasia) represents a condition which is commonly accepted as a malignant clinical condition. The second cytoplasia (secondary cytoplasia) with our present knowledge is still doubtful as to malignancy or benignancy and represents a group which has been variously considered by both pathologists and clinicians—a group which has caused endless confusion to the pathologist and clinician.

9. Biologically certain regenerative cells react to irritation which destroys the end-products of their specific differentiation: (1) by hypertrophy, (2) by hyperplasia, and (3) by migration.

The terminology of the classification which is herewith presented consists of well-known and accepted terms. It expresses in its first word the stage of cytological activity in response to irritative stimuli; the second word denotes the tissue the regenerative cells of which are involved in the neoplastic condition; the third word is merely a term which signifies condition of cells. Thus by such

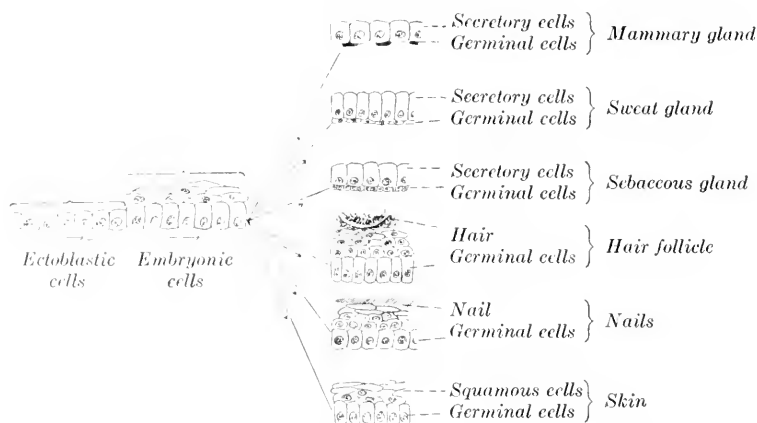


FIG. 7.—Cytological differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat glands, sebaceous glands, hair, nails and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin and the epidermis of the skin.

an expression as primary fibrocytoplasia is meant that there is a condition of primary reaction of the regenerative cells of fibrous connective tissue.

In a primary reaction there is an attempted if not complete reproduction of the specific cells. In a secondary reaction there is a failure to reproduce specific cells plus an overgrowth of regenerative cells. In the third reaction there is a migration of the hyperplastic regenerative cells. Each one of these cytoplasias is expressed by terms the etymology of which is well known and accepted in biology. Thus:

I. Primary (restauro-) . . .	{ fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x- }	cytoplasia.
II. Secondary (expando-) . . .	{ fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x- }	cytoplasia.
III. Tertiary (migro-) . . .	{ fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x- }	cytoplasia.

The term polycytoplasia is utilized to express a neoplastic condition in which all or many of the tissues are present, such as in teratomas and dermoids.

The term x-cytoplasia is the convenient term for grouping cytoplasia, the tissue origin of which is unknown.

CONCLUSIONS. 1. This classification, which is in accord with biological terminology and conception, standardizes the science of neoplasia and allows complete correlation of clinical observation with cytologic activity.

2. It forms the basis of an accurate determination of the clinical value of pathological data.

3. It will eventually expel the clinician's pessimistic idea of the work of the histopathologist, who by means of his lack of standardization has certainly incurred severe and detrimental criticism.

## SAPHENOPERITONEAL ANASTOMOSIS FOR ASCITES.

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WHEN Ruotte,<sup>1</sup> in 1907, suggested that ascitic fluid be drained off into the general circulation by means of a union between the saphenous vein and the peritoneal cavity, he provided a method of exit not only medically sound and mechanically correct, but one quite feasible as well. It may be theoretically more advisable to prevent the occurrence of an ascites by providing a collateral circulation which will relieve the congested portal apparatus—as carried out in the Talma operation—but the building of such pathways is never certain of accomplishment even under the best of circumstances. Furthermore, the results obtained in those cases in which trial has been made with this end in view leaves much to be desired—the operation either fails of its purpose entirely or only partially succeeds—and not infrequently the patient succumbs in the attempt.

It is unnecessary to discuss the many other measures which have been suggested for the relief of this distressing malady, since most of them have been too theoretical for practical purposes and all of them have been tried and found wanting, except possibly in a very few selected instances. The crux of the matter then is about as follows: an individual, for one cause or another, suffers an obstruction to his portal circulation which results in the pouring out of a tremendous amount of serous exudate into his peritoneal cavity from which it cannot be absorbed. Simple as it is to relieve him of this collection by tapping, it can readily be seen that con-

<sup>1</sup> Saphenoperitoneal Anastomosis for Ascites, *Lyon Médicale*, 1907, No. 40; *Semaine Méd.*, 1909.

tinuous tappings over a lengthy period will not do because the organism cannot withstand the great loss of fluid thus suffered. The problem then is how to restore this fluid to its normal channels. Routte suggested the use of the saphenous vein, and his method of procedure was to dissect it out for a distance of a few inches from the saphenofemoral opening, cut it in two at the lowest point, tie off the distal end and turn the proximal end up toward the abdomen. Having undermined the subcutaneous tissues overlying Poupart's ligaments, he made an incision through the skin, fascia, and abdominal muscles, drew up the peritoneum, cut a small hole in it to correspond with the opened end of the saphenous vein and did an anastomosis between the two. He suggested that the procedure be done on both sides at one or two sittings, as most convenient.

About twenty-five<sup>2</sup> of these cases have been reported, all, so far as I am aware, having been done abroad.<sup>3</sup> No attempt at special selection of cases<sup>4</sup> was made and the operators<sup>5</sup> had no unusual skill in bloodvessel suturing, yet the result was most promising, since in about one-half a marked improvement was secured. In some instances patients who had been bed-ridden were enabled to resume their occupations. Why a more general use has not been made of the procedure or what results a wider trial would bring forth cannot be surmised. The operation can be done with impunity, lends itself readily to local anesthesia, and causes little or no shock.

**CASE REPORT.**—The case I wish to present was as follows: Mr. M., aged sixty-eight years, referred by Drs. Omar Pancoast and Frederick Leitz, had suffered from ascites for over a year, the cause being an obstruction of the portal vein consequent on a cirrhosis of the liver. Dr. Pancoast had done a Talma operation some months previously without relief. Repeated tappings were the order of the day, at each tap several gallons of fluid being removed. The depletion thus suffered, the rapid reaccumulation of fluid and the hopeless aspect of his condition in general finally began to tell on the patient to such an extent that he was willing, he even pleaded that something be done that promised possible permanent relief.

Accordingly, on April 25, 1915, under local anesthesia, I exposed the patient's left saphenous vein for a distance of about six inches and cut it off at the lower end of the wound, tying off both ends (Fig. 1). Fortunately for our purposes a large inguinal hernia was present, so it was quite simple to expose the peritoneal sac through a two-inch incision just over the external ring, at which point a very

<sup>2</sup> Morosawa, A. J., Die Ruottische Operation bei Ascites, *Centralbl. f. Chir.*, 1913, No. 4.

<sup>3</sup> Simon, Ueber Ruottische Operation, *Berl. klin. Wchnschr.*, 1913, No. 32.

<sup>4</sup> Schwarzman, Zur Chirurgischer Behandlung des Ascites, *Deutsch. Ztschr. f. Chir.*, Bd. cxxiv, H. 5 u. 6.

<sup>5</sup> Permiöff-Kasan, *Centralbl. f. Chir.*, 1913, No. 4.

small hole (about 12 cm.) was made and the greater part of the ascitic fluid that was present—two gallons—was drained off (Fig. 2). This done, the tissues overlying Poupart's ligament were undermined by means of a curved clamp, and the proximal end of the severed vein pulled up into the small incision, where a lateral anastomosis was done between the bloodvessel and the peritoneum, ordinary bloodvessel silk (No. 00000) being utilized (Figs. 3 and 4).

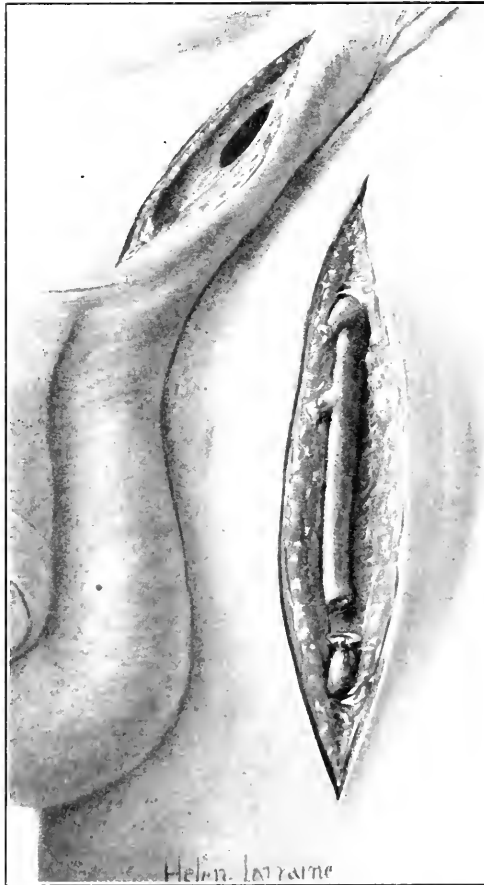


FIG. 1.—Saphenous vein exposed. Its distal end ligated.

Prior to the suture it was noted that the vein valves were competent—that is, allowed no back bleeding. And the patency of the vein lumen was definitely established by running a few cubic centimeters of salt solution through it into the general circulation by means of an ordinary Record syringe. The only disturbing feature was the apparent small caliber of the vein, it being only



about one-half normal diameter, although its wall was quite soft and normal in every respect.

A lateral anastomosis—accomplished without great difficulty—was preferred to the usual end to side because of the greater ease of operative performance. Both wounds were closed in the usual

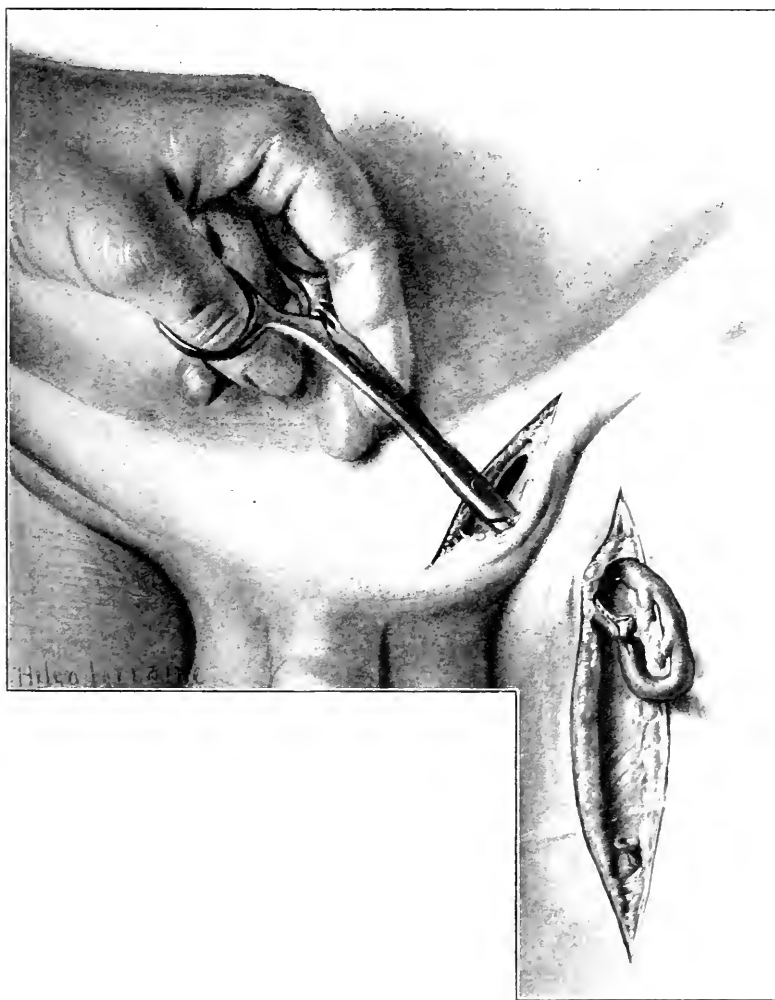


FIG. 2.—Incision through peritoneum. Vein being pulled through undermined fascia.

manner and the patient left the table in good shape. It had been my original intention to do both sides at one sitting, but owing to the patient's great age and poor physical condition, and the fact that the right leg was markedly edematous, it was deemed best to do but the one.

For twenty-four hours all went well, but the patient insisted on getting on his feet to urinate—as had always been his custom—and the result was leakage at the site of the suture, probably due

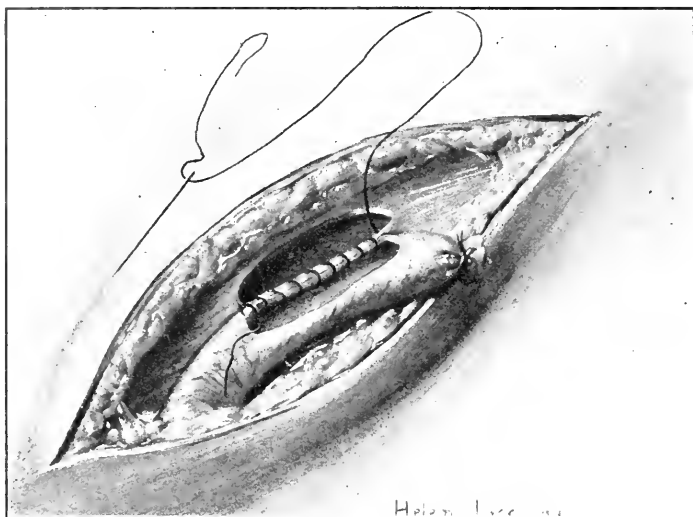


FIG. 3.—Peritoneum and vein being united.

to the great strain put upon it, since all of the ascitic fluid had not been withdrawn. This leakage continued for two or three days, until finally I compelled the patient either to be catheterized or to

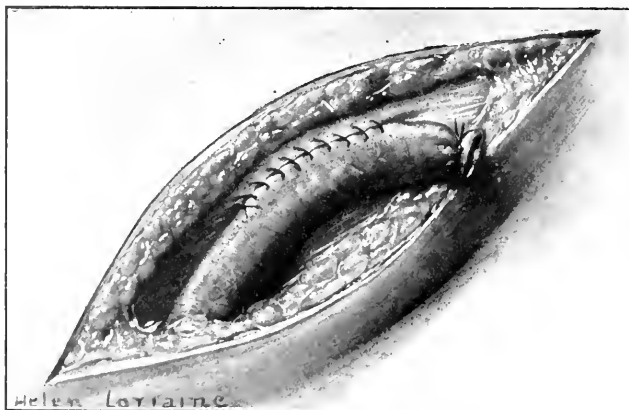


FIG. 4.—Anastomosis completed.

pass his urine in the recumbent position. He did the latter, and, the foot of the bed being elevated, the leakage promptly ceased. Thus matters progressed, temperature but slightly elevated, wound

in good shape, and patient apparently in good condition, until midnight of the eighth day, when he complained of pain in his right shoulder. He had had similar pains in this shoulder frequently before coming into the infirmary, so but little was thought of the matter, and he was given a hypodermic injection of morphin, gr.  $\frac{1}{6}$ . Early next morning he was given by hypodermic  $\frac{1}{8}$  gr. of morphin, and an hour or so later, his pain being still unrelieved, this was repeated, when by chance his nurse found a small bottle of morphin tablets (gr.  $\frac{1}{4}$ ) under his pillow. Questioned as to where he had gotten them, he said they had been given to him some weeks previously by his physician, and he had been in the habit of taking an occasional one as needed. He claimed that he had not taken any of the tablets during this last attack of pain, but whether he did or not the fact remains that gradually during the morning he went off into a semiconscious stuporous state from which he could be aroused with difficulty. His pupils were a bit contracted, he was rather cyanotic, and seemed to have a certain degree of air-hunger. A careful examination failed to reveal the slightest degree of dilatation of the heart. In fact, no cause whatever could be found for this patient's death, which took place about sixteen hours after the initial attack of pain in his right shoulder. His bowels had been in good shape and he had been voiding, apparently, a sufficient amount of urine. Whether this was a death from morphin poisoning or not cannot be told with certainty. It does not seem possible however, that the man died from his operation. There was no symptom of an embolus nor was a demonstrable pneumonia present.

The family refused permission to do an autopsy or even an exploration at the site of the wound, although every effort was made to secure this permission, and all sorts of influence brought to bear. This was most unfortunate, since considerable light might have been thrown on the case and valuable knowledge for future guidance might thus have been secured. It seems fair to conclude, though, that the operation is worthy of further trial in suitable cases, since technically it is not difficult to carry out, and theoretically it has much to commend it.

## THE THERAPEUTIC POSSIBILITIES OF ANTITETANUS SERUM.

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(From the Pathological Institute, University of Freiburg in Br., Prof. L. Aschoff, Director.)

It is a generally recognized fact that tetanus antitoxin may be employed in two ways: (1) as a prophylactic measure, having for

its object the prevention of a possible outbreak of tetanus,<sup>1</sup> and (2) as a therapeutic agent for combating the toxin of this disease after symptoms have already appeared. While these two divisions of the subject each require special consideration, it must be recognized at the outset that the principles which underlie both applications of the serum are exactly the same.

In both we are concerned with a foreign serum which when injected into the body, no matter whether under the skin or into the cerebrospinal canal, in a comparatively short time is absorbed from the tissue spaces into the blood stream, from which in turn it is later partly distributed to the general lymph circulation and partly excreted. Knorr found in animal experiments that the maximum amount appeared in the blood stream twenty-four to thirty-six hours after subcutaneous injections. From that time the amount steadily decreased until on the sixth day only about one-third and on the twelfth day one fifty-fifth of this quantity was present, while at the end of three weeks none at all could be demonstrated. Behring showed that after injecting a definite amount of tetanus antitoxin into the blood stream this amount remained practically unchanged for about one hour, after which time it gradually began to decrease. Indeed so confident was he of this retention of antitoxin in the blood stream that he proposed that such injections should be used, both in man and in animals, as a means of determining the amount of blood in the body. The value of this new method has been repeatedly confirmed, among others by Zangemeister, Matthes, Friederick v. Müller, and Kämmerer and Waldmann.

The disappearance of antitoxin from the body follows in general those laws which govern the disposal of any foreign serum *in vivo*. Behring was able to demonstrate its presence in the urine and intestinal secretions of passively immunized guinea-pigs, and Vagedes claimed to have found it in the urine of a man who had been treated with antitoxin. Brieger and Ehrlich investigated the milk of nursing animals which had received injections of serum, and discovered that appreciable quantities might be excreted in this manner. Tizzoni and Cattani, among others, have shown that it is able to pass through the placental bloodvessels in a preg-

<sup>1</sup> One must not, however, confuse prophylaxis in tetanus with, for example, vaccination in smallpox or typhoid fever, which, while they are also prophylactic or protective measures, depend entirely for their protection upon reactions which occur, *intra vitam*, between the vaccine and the tissues and fluids of the body, by which reactions newly formed protective substances are produced which are capable of warding off the diseases for which they are specific. The protection afforded by such vaccines often lasts for years. Tetanus antitoxin, on the other hand, the same as diphtheria antitoxin, is a finished product, capable of at once neutralizing its specific toxin no matter whether the contact between the two occurs within the body or *in vitro*. As would be expected the protection obtained from such a serum is comparatively transitory. This phase of the subject (prophylaxis) has been fully treated in a previous article.

nant animal and can then be demonstrated in the blood of the offspring. Undoubtedly a considerable amount is destroyed in the body, this destruction probably taking place both in the blood stream and in the tissue fluids. The phenomena associated with so-called "serum Krankheit," or anaphylaxis, are supposed to depend upon the action of a ferment which is capable of splitting up the antitoxin molecule. In a case of myelogenous leukemia, Kämmerer and Waldmann noted that it disappeared more rapidly than usual from the blood, due, as they suggested, to the increased tryptic activity of the leukocytic ferments.

Naturally in the disposal of this serum the lymph plays an important role. Ransom was able to find traces of antitoxin in the ductus thoracicus of a dog a few minutes after intravenous injection, and also showed that while it was later present in the cerebrospinal fluid and nerve lymph the amounts were always less than those in the blood stream. As would be expected the proof of its presence or absence in the tissue spaces of the brain and spinal cord is exceedingly difficult, because the well-known antitoxic properties of these tissues themselves would obscure the results of any of the usual test methods. However, it is reasonable to suppose that since it passes over into the lymph stream and is present in the cerebrospinal fluid and nerves it must also penetrate to the tissue spaces of the brain and cord if only to a limited extent.

When tetanus antitoxin, then, is injected into the body by the subcutaneous or intralumbar methods it is rapidly absorbed into the blood stream and the processes of excretion and destruction cause it to disappear entirely from the body in a few weeks. By intravenous injections, on the other hand, it is more rapidly distributed throughout the entire body and also more quickly passes from the blood into the general lymph circulation. Its greatest concentration, however, excepting only the local point of injection, is always in the blood stream.

Having reviewed the conditions under which tetanus antitoxin remains in the body, we are better prepared to consider its employment in the cure of tetanus after symptoms have once appeared, *i. e.*, its therapeutic possibilities.

In an attempt to reach a correct judgment of the value of tetanus antitoxin as a therapeutic or curative agent, the pendulum of both experimental and clinical medicine has swung from one extreme to the other. One naturally expected at the outset that its effect on the mortality of tetanus would be equal to that of diphtheria antitoxin on the mortality of diphtheria, and Behring confidently predicted that provided the serum was given early enough (within thirty hours after the first symptoms appeared) and in large enough doses (100 units, German standard) the death rate could be reduced to as low as 15 to 20 per cent. It is not our purpose to review here the statistical evidence on this question. One needs

only to consult the extensive reports of Steuer, Engelmann, Köhler, Lemonnier, Vallas, Chattot, Jacobson and Pease, Ullrich, Permin, and others to form a fairly accurate estimate of the results of the study of large collections of treated cases. Certainly the earlier expectations have not as yet been realized and the general clinical opinion in this regard is today decidedly pessimistic.

In the laboratory and on the theoretical side the same differences in results and opinions have appeared. Knorr by carefully graduated doses of tetanus toxin and antitetanus serum was able to save the lives of laboratory animals by beginning treatment as late as thirty-six hours after the injection of toxin and twenty-four hours after the appearance of the first symptoms. In order to meet the possible objection that the injection of artificially prepared tetanus toxin does not compare with the conditions of natural infection, he also used splinters of wood inoculated with tetanus spores, and by placing these under the skin of guinea-pigs he could still save their lives by the use of repeated large doses of serum given first as late as four days after the inoculation and thirty-six hours after the first symptoms had appeared.

These results have not been confirmed by the researches of most other workers. For example, Roux and Vaillard as well as Beck were unable to save animals if the treatment was not started before symptoms first appeared. Also in my own earlier experiments, which were directed toward establishing the therapeutic value of antitoxin, the results were fully as discouraging. As a rule it was necessary to give antitoxin under the skin at least two hours before the injection of toxin if we would save the animal's life. In the very occasional cases in which antitoxin was given first after symptoms of tetanus appeared, and the animal survived, the symptoms were always slow in advancing toward the upper parts of the body, *i. e.*, they were for a comparatively long time confined locally to one or both hind legs.

Hence it becomes very important in this connection to keep in mind the differences between laboratory and human tetanus. Most of the laboratory animals (guinea-pigs, rabbits, rats, mice, etc.) after a subcutaneous or intramuscular injection of tetanus toxin or inoculation of tetanus spores in the hind leg show a local tetanus or "tetanus ascendens" (Zupnik), *i. e.*, the toxin is first and in large part taken up by the lymph channels of the motor nerves of the inoculated extremity and thus conveyed to the corresponding centres in the spinal cord, from the poisoning of which centres entirely local spastic phenomena are first produced. It is not until many hours (twelve to twenty-four) later that the centres governing the opposite limb and those lying higher in the spinal cord become affected, and only after the lapse of several days do the respiratory levels begin to show evidences of intoxication. In fact, in these animals the vital centres are usually the

last to suffer attack. For some unknown reason the main path of travel for the toxin is up the spinal cord, and only relatively small amounts of toxin appear to be distributed by the blood stream to the other motor nerves of the body.<sup>2</sup>

This peculiar reaction is largely a property of certain animal species, not being shared by all animals alike, *e. g.*, the frog never shows local tetanus (Gumprecht). It probably depends upon the movements of the lymph currents in the nervous system and their relation to the capillary blood circulation of the muscles, as well as the varying degrees of sensitiveness of the various centres in the spinal cord and brain to the influence of tetanus toxin. By injecting tetanus toxin into the blood stream of a rabbit or guinea-pig, or subcutaneously into the tip of the toe (Zupnik), symptoms more generalized and often approaching in type those seen in man may be produced. Even here, however, the resemblance is only superficial, for not only can toxin be shown to have early invaded the sciatic nerves (Meyer and Ransom), but the spasmodic cramps, at least in the first stages, are much more intensive in the hind-quarters.

In man, on the other hand, no matter where the site of the infection may be located, the first symptom is usually *trismus*, *i. e.*, the motor centres which lie near the most vital centres of the nervous system are the first to be attacked. The further progress of the disease follows that of a tetanus descendens, or, better, a general tetanus, and is comparatively rapid in its development. The toxin, instead of largely passing to the spinal cord by the peripheral nerves of the injured part, is rapidly absorbed into the blood stream, and from this is first conveyed to the nerve centres either directly or by the nerves of the face and neck.<sup>3</sup> Zupnik believed these facts could be explained by the varying reaction between opposed groups of muscles, while Pochhammer suggested that the condition was due to the comparative shortness of the upper spinal nerves, and endeavored to show that, in general, the length of the nerves regulated the time of the appearance of symptoms. The difference exhibited by the various animal species, however, in their reactions to tetanus toxin can hardly be explained on this basis, and I am more inclined to offer the above-mentioned possibility, namely, a varying degree of sensitiveness of the various centres for tetanus toxin.

<sup>2</sup> Meyer and Ransom hold that tetanus toxin, at least in animals, is never directly absorbed from the blood into the central nervous system, but always passes indirectly by means of the peripheral nerves. It is difficult to determine to what extent this holds true. As Permin emphasizes, both the indirect passage through the nerves and the direct absorption from the blood must be granted as theoretical possibilities.

<sup>3</sup> Cases of fairly typical tetanus ascendens or local tetanus are also described as occurring in man, and have been carefully reviewed by Sawamura. Not only are such cases rare, but they are usually mild in their course and symptoms, *e. g.*, of the 12 cases collected by Sawamura, 8 recovered.

From these facts it is clear that the results obtained by the administration of tetanus antitoxin to animals in cases of tetanus ascendens cannot rightfully be used as a measure upon which to judge of the exact treatment required and justified in human cases. In laboratory animals not only is the toxin in the blood neutralized, but undoubtedly, in many cases, its advance in the lymph spaces of the nerves and spinal cord can be brought to a standstill. This latter result is probably also influenced by the fact that the chemical combining power, which fixes toxin to the ganglion cells of the spinal cord, in tetanus ascendens, is, at first, largely exerted by the cells in the lower levels, so that the amount of toxin in the early stages is markedly diminished by its union with lower and less vital centres of the cord. On the other hand, in man, when the first symptoms have appeared, the vital centres, as a rule, are already in grave danger, and in a large percentage of cases, especially those with an incubation period under six days, it is very doubtful if any means whatsoever will avail to preserve these centres from attack.

Our main efforts must, then, be directed toward the neutralization by antitoxin of the toxin which is present in the blood stream, and that which may be further produced and thrown into the blood.

One can hardly hope in man to overtake and render harmless that toxin which is already in the lymph channels of the nerves or the lymph spaces of the central nervous system or that portion which has become united with the nerve cells and has brought about the initial symptoms. Theoretically if one could inject antitoxin into each of these nerves or into the threatened regions of the cord and brain the small percentage of toxin still present in these lymph spaces might be neutralized; practically such measures are, of course, absolutely out of the question. The injection of nerves in the injured extremity, such as the sciatic, so effective in the local ascending tetanus of laboratory animals, in human beings serves very little if any useful purpose. Such injections do not distribute antitoxin directly to the rest of the spinal cord—they only serve to protect the corresponding centres of those nerves which are injected—and not only are the motor centres of the extremities not vital centres, but their nerves in man are not the most important conductors of tetanus toxin to the cord and brain. The very best one can do is to render harmless, at the earliest possible moment, the toxin circulating free in the blood and to make impossible the circulation of any further toxin. For this purpose the intravenous injection of antitetanus serum is, as v. Graff emphasizes, a nearly perfect remedy, and, moreover, is not demanded in overwhelming or even large doses.

In the endeavor to cure experimental tetanus in animals one aims toward forcing a high concentration of antitoxin into the lymph fluids, toward driving antitoxin into the lymph spaces of



the nervous system—in short, to overwhelm the body with large doses of antitoxic serum with the expectation of preventing the onward march of tetanus toxin toward the threatened centres of respiration. In these laboratory animals such a procedure is also theoretically more or less justifiable, for, as explained, the toxin advances rather slowly from below upward, so that flooding of the body and, thereby, to a certain extent the central nervous system, with antitoxin may be the means of preserving the animal's life. In man, on the other hand, such measures not only serve no useful purpose but are a waste of good antitoxin.<sup>4</sup> This surcharging of the lymph spaces with antitoxin is distinctly a time-consuming process, for the antitoxin molecule, perhaps due to its comparatively large size, does not readily pass unchanged through the excreting and secreting membranes of the body. By the time the nervous system has been flooded it is too late—tetanus toxin, in man, after the appearance of symptoms, is already in the region of the vital centres of the medulla and only a minimal lapse of time suffices for a fatal intoxication.

To overcome this difficulty, several "short cuts" have been proposed. Roux and Borrel suggested that the serum be injected directly into the brain substance. Not only has the method proved to be a dangerous operation, but it has very little rational basis for its justification. In animals, perhaps, for the reasons explained above; in man there is little reason to suppose that it does more than protect its local area from toxin invasion, while the surplus is, in turn, absorbed into the blood stream and then follows the usual path of antitoxin introduced in other ways. It may be freely granted that if the injection could be made into the region of the "danger zone" a certain amount of protection might be effectively produced. However, naturally the danger from the toxin would only be substituted by the equally pressing dangers incident to the injection itself.

Blumenthal and Jacob first advocated intralumbar injection of antitoxin, hoping thereby to exert a more direct and quicker action on the toxin in the nervous system. Here, again, in laboratory animals the procedure was accompanied by good success, and hence found wide acceptance in the treatment of human cases. There can be no doubt that in such animals the method possesses certain advantages over some others, *e. g.*, subcutaneous injections. Gumprecht was able by this means to block off the nerves of the lower extremities so that the corresponding spinal cord centres were protected against the advance of tetanus toxin. Meyer and Ransom confirm Gumprecht's experiments, but they also insist

<sup>4</sup> When, however, for his own peace of mind and with the hardly justifiable hope that the toxin then present in the lymph channels of the nervous system may yet be neutralized, the physician feels that he must resort to a large dose, this should, if it is to accomplish any good purpose, be given intravenously and not subcutaneously.

that the antitoxin so injected is promptly absorbed into the blood stream and has little or no effect on the toxin present in the spinal cord. But, granted that the lumbar level of the cord could thus be protected, this is not the "danger zone," and is far removed from it. Just as with the intracerebral injection, if the antitoxin could be introduced into the cervical region of the spinal column, as suggested by Jonnesco, the slight advantage gained in combating the toxin in the lymph channels of the nerves would be more than counterbalanced by the dangers of the operation.

Permin has proposed as a possible modification of the subarachnoid injection the lowering of the patient's head to as near the vertical as possible, hoping thereby to bring the serum, through the action of gravity, into contact with the cervical nerve roots. In animal experiments this method proved to be a slight improvement over the usual intralumbar injections, but even here it was necessary to give the antitoxin not later than six hours after the toxin in order to save the animals. To say nothing of the doubtful practicability of this procedure in human beings, there would be an evident loss of time in bringing the antitoxin into the desired regions of the subarachnoid space, and it is this loss of time, when every minute may mean a serious difference in the outcome of the case, that we wish by all means to avoid.

Early in his work on tetanus antitoxin, Behring recognized the theoretical advantages of the intravenous injections, but he exhibited a distinct hesitancy toward giving this method his unqualified indorsement. This hesitancy evidently, in part at least, proceeded from a fear of the dangers incident to the injection of a foreign serum into the body and a belief that these dangers were more threatening with intravascular than with subcutaneous administration. It is true that with extensive use of diphtheria antitoxin, cases of "serum Krankheit" became fairly common, and in a small percentage of cases threatening symptoms of asphyxia and even death followed its use. While, however, the occurrence of urticaria and other skin phenomena, following the administration of tetanus antitoxin, is well known, there are, so far as we have been able to find, very few records of "serum death" which really resulted from its use. Not only has the work on anaphylaxis or proteid reactions shown that there is little difference to be observed as regards the method of injecting the foreign proteid, but with the present purification and concentration of modern antitoxic serums this danger has been reduced to a negligible minimum.

On the contrary the subcutaneous method has met with much more favor from the clinical world, and largely because of its simplicity and ease it may be said today to be the one most usually employed. It should be distinctly emphasized that for therapeutic or curative purposes, *i. e.*, after symptoms have appeared, this method is a useless and irrational waste of precious time. All local subcutaneous injections of antitoxin are able fully to protect the

local area from toxin. But our main purpose is not to protect the local area, but to reach the toxin circulating in the blood.

I propose, therefore, that every case in which symptoms of tetanus appear be treated at once, without delay, with an intravenous injection of 3000 units<sup>5</sup> of antitetanus serum. The "at once" should be emphasized. Even the saving of minutes of time may mean the difference between the life and death of the patient. The experiments of Donitz and others show with what exceeding rapidity toxin travels in the body and how soon it passes in part beyond the reach of all antitoxin. It is not believed that by this or any other known therapeutic procedure the lives of all or even of any large proportion of tetanus patients can be saved. Prophylaxis is, as has been shown,<sup>6</sup> the only means known at present which can bring the death rate in tetanus to anywhere near the zero point. It is desired here merely to emphasize that by this method every patient who exhibits the symptoms of tetanus is given the best possible opportunity of preserving his life. Difficult or dangerous surgical operations, such as the intracerebral method or intralumbar injection, need not be considered; the loss of time and local pain of subcutaneous injections are avoided, and, what is of less theoretical, but nevertheless often of more practical serious moment, the use of large amounts of serum is obviated. The method consists simply in the immediate insertion of 3000 units of antitoxic serum into one of the veins of the elbow.<sup>7</sup>

<sup>5</sup> In the work of Aschoff and Robertson twenty antitoxin units (German standard) was suggested as the unit dose for intravenous injection in cases of outbroken tetanus. This amount was more or less arbitrarily fixed. It is, for one thing, in Germany the usual prophylactic dose, and is held in bottles containing exactly this amount. The amount of antitoxic serum which neutralizes an amount of test toxin which would destroy 40,000,000 grams of mouse contains 1 unit of antitoxin by the German standard. In the United States a unit is defined as the amount of antitoxin required to just neutralize 1000 fatal doses of tetanus toxin for a 350-gram guinea-pig. Supposing both mice and guinea-pigs to be equally susceptible per gram weight to tetanus toxin, it may at once be seen that the German antitoxin unit is about one hundred and fifteen times as potent as that of the United States. If we should accept the work of Behring, who states that a guinea-pig is six times as sensitive to tetanus toxin per gram weight as a mouse, then the German unit would be correspondingly greater in neutralizing power. However, the figure 3000 has been selected in this country as representing an approximate equivalent to the original figure.

<sup>6</sup> Robertson, *The Prophylactic Use of Tetanus Antitoxin*, AMER. JOUR. MED. SCI., May, 1916, p. 668.

<sup>7</sup> In this connection must be noted the theoretical possibility that at the time of the injection of antitoxin there may be no toxin then present in the blood stream. There are many facts which indicate that the formation and absorption of toxin occurs, under usual conditions, in the early days of a tetanus infection, and that then both the presence of granulation tissue and the exhaustion of the bacillus' growth or toxin forming ability greatly diminish or even entirely prevent further entrance of toxin into the blood and lymph streams. Also, Pochhammer claims (p. 683) that "each tetanus patient, either man or animal, at the time of the outbreak of symptoms often already possesses in his blood serum large quantities of antitoxin." If one could be certain in any given case that either of these conditions prevailed, the intravascular injection of antitoxin (or administration by any other method) could have no reasonable purpose. However, not only has little proof been advanced for Pochhammer's assertion, but, on the contrary many times (among others by Nissen, Brunner, Buschke and Oergel, and Symanski) the presence of tetanus toxin has been demonstrated in the blood. On the whole, we must follow those rules in treatment which give the most reasonable expectation of success.

Furthermore it is of little or no value to repeat this dose twice a day or every other day or, in the large majority of cases, at all. The one injection of 3000 units is amply sufficient to neutralize the toxin which might be elaborated and absorbed from any ordinary tetanus infection, and this antitoxin will remain effective in the blood stream for at least one week, *i. e.*, long enough to decide the issue in almost all cases of human tetanus. If the case should become chronic or suffer a recurrence or any other special condition should develop which might indicate the advisability of giving more antitoxin, there can be no objection to a second or even a third dose; but here again it should be emphasized that a small dose is fully as effective as a large one and a large dose is as unjustifiable the second time as it was the first.

In conclusion, I should like to be certain that undue emphasis shall not be placed upon the element of dosage. The proposal is that as soon as symptoms of tetanus have appeared, 3000 units of antitetanus serum should be injected at once into the circulation. The immediate intravascular injection is the important feature and the amount of the dose a purely secondary matter. Personally I am fully convinced, for reasons which cannot be discussed here, that one-half this amount would be just as efficacious. Twice this dose, however, can do no harm. The main stress is here laid upon the recognition of the theoretical considerations which underlie the therapeutic application of antitetanus serum and a rational *modus operandi* based upon these principles.

Naturally the complete treatment of the disease involves the application of many other measures the consideration of which does not come within the scope of this paper, but will be fully discussed in a later article.

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**INTESTINAL STASIS.**

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THE treatment of intestinal stasis can no longer be relegated to the realm of empiricism but demands an individual study of each case, including a careful history—physical, laboratory, and, in many instances, Roentgen-ray examination.

Regarding the history, there are some general points which at first may sound trivial, but which often have a profound bearing on the case. Among these is the mode of living. Many men and women suffer from habitual constipation simply through lack of regular habits; men who commute, eat their breakfast with an eye on the clock and before the last mouthful is swallowed, seize hat and coat and rush for a train. Some young women, either from diffidence or lack of proper hygienic education, never seek the toilet until the demand becomes imperative. The inclination to defecation being resisted, the desire soon passes away and often does not occur again until the next regular period.

It is this voluntary inhibition of defecation, with its consequent retention of feces, that leads to the blunting of the sensibility of the rectum, and is one of the most potent factors in the production of a common variety of stasis.

The human intestines, as a rule, evacuate their contents every twenty-four hours, usually after breakfast, although there are exceptions to this in apparently healthy persons, who defecate at intervals of forty-eight hours to four or five days; but they are the exception. This desire to defecate after breakfast is partly habit, but due more to the stimulus of food entering a completely empty stomach and starting intestinal peristalsis.

The intestinal movements under certain conditions are inhibited by nervous influences. Thus, Cannon found that intestinal movements in cats ceased when they were excited or angry.

Much of the activity of the intestines depends on the chemical as well as the mechanical stimulation of the food, its digestion, and its bacterial decomposition.

Vegetable food is more important than animal, both on account of the mechanical irritation and because of its stimulation through fermentation.

The question in treating any case of stasis is to find out the etiological factor or factors.

A careful history, as has been said, is the first essential. The examination of the abdomen, rectum, stool, urine, and possibly a Roentgen-ray follow as a routine measure.

In examining the abdomen the following points should be especially noted:

The *habitus*, namely, the degree of the costal angle. Such cases presenting the so-called *habitus enteroptoticus*, with the narrow costal angle and generally poor muscular development, have a tendency to visceral ptosis with its resulting kinks and angulations. Again, such persons are much more prone to constipation than are those with a normal, well-developed *habitus*, owing to a weakness of abdominal and pelvic muscles.

The former teaching that constipation was the result of colonic atony or spasm is, in the light of more recent work, no longer tenable. Holtzknack, Hertz, A. E. Barclay, and others have shown that the intestinal propulsion of contents is not a slow, gradual process, but one which they term "mass movements," namely, a sudden forward movement of the entire fecal mass, the action being exceedingly rapid. Holtzknack has reported an observation where the head of the bismuth column was in the region of the hepatic flexure, and when the movement finished, which took about three seconds, the head of the bismuth shadow had advanced beyond the splenic flexure. This mechanism appears to be: (1) a relaxation of the tonic action of the muscular coats; (2) followed by a big peristaltic wave that sweeps the whole contents along. The movement probably occurs three or four times a day, and it is strongest after breakfast when food is received in the stomach after a night's fast.

Leaving out of consideration the question of kinks and angulations and inflammatory conditions, such as a chronic appendix, we recognize two main types of constipation: (a) that occurring in the sigmoid and rectum; (b) that occurring in the cecum, which has been termed "true constipation," and is due to a failure of the mass movement.

The former, *i. e.*, rectal constipation, is much more common.

It is highly improbable that the cecum has any part in the forward propulsion of feces. This portion of the gut apparently has a separate mechanism or peristalsis for the mixing of contents and feeding them into the ascending colon preparatory to the occurrence of the "mass movement."

Hertz attributes the dilated splashing ceca to the result of a failure of the forward mass movement, the intestinal contents regurgitating back into the cecum, causing an inflammatory reaction which results in relaxation and absorption of the mucosa and muscular coats, and that such ceca are the results and not the cause of constipation.

The cecal or "wet constipation," as it has been called, is liable to be associated with symptoms of toxemia, while, on the other hand, the rectal and sigmoid type, which has been termed "dry constipation," is rarely associated with any toxic symptoms.

When we come to consider the etiological factors in these types of stasis the whole problem is wrought with many difficulties, for it must be realized that the large intestine is but one part of a complex organization so closely linked together by nerve-centre relays and subcentres that it is almost impossible to separate the constituent anatomical parts and deal with them separately.

Whether these sloppy ceca are the result of faulty mechanics or bacterial infection is still undetermined; the general feeling is one of faulty mechanics, the inflammation and infection being secondary.

**ILEAL STASIS.** In 1903 Arthur Keith demonstrated the existence of a strong ileocecal sphincter in man; he suggested, and his observations have been borne out by others, that the function of this sphincter is to prevent the contents of the ileum from passing too rapidly into the cecum and not, as has been suggested by some observers, to prevent antiperistaltic waves, which do not normally occur in the ascending colon, from passing feces from colon to the ileum.

Alan Newton and Hertz showed that bismuth containing chyme reached the end of the ileum an hour or longer before any appreciable quantity passed into the cecum, and that the ileum is still full four to seven hours or more after the last trace of bismuth has left the stomach, consequently an accumulation of chyme occurs in the last few inches of the ileum, where it remains and undergoes digestion for a longer period than in the stomach; this ileal stasis, up to a point, is a physiological condition.

Normal ileac stasis is increased in all conditions leading to spasm or to the inhibition of the normal relaxation of the ileocecal sphincter.

In acute appendicitis, for example, the sounds which normally indicate the squirting of the contents of the ileum into the gas-containing cecum cease completely, owing, probably, to spasm of the sphincter.

Also an accumulation of feces in the cecum will give rise to back pressure, and in every case of cecal constipation one will see evidence of ileal stasis. Thus the necessity of having the colon well cleaned before attempting to make a radiographic diagnosis of ileal stasis.

Stasis of the terminal ileum can result, according to Lane, from a thickened mesentery band supporting the terminal end of the ileum, while the cecum and remaining portions of the small intestine are allowed to sag in the pelvis.

Lane, as is known, further maintains that the pull exerted by the prolapsed small intestine exercises, through the medium of the



jejunum, a strain on the termination of the duodenum, producing a kinking at the duodenojejunal junction, and giving rise to a partial obstruction at the terminal portion of the duodenum.

It would seem, from numerous radiographic studies, that ptosis of the intestines alone does not lead to stasis, except in rare instances at the splenic flexure, from too acute angulation.

In fluoroscopic examination of the colon it often appears as if there were exceedingly sharp angles at the hepatic and splenic flexures, but this would seem to be due more to the shadow being cast in a single plane, for when viewed from the side they form a wide angle.

Adhesions involving the limbs of the hepatic and splenic flexure can almost always be determined by ascertaining if they can be separated by palpitation during the fluoroscopic examination. I have observed numerous pelvic ceca and transverse colons in patients whose bowels were functioning normally, and in my opinion such cases of ptosis are not in themselves sufficient to cause stasis.

A ptosis of the transverse colon, in my experience, never leads to kinking at the hepatic flexure, although an enlarged and prolapsed right kidney has been known to produce obstruction by pressure at this point.

As a rule, in most cases of constipation, a single part of the bowel, such as the rectum, pelvic colon, ascending colon, or splenic flexure, is involved, and treatment should therefore be directed to that part, and many of these conditions require surgical interference.

In those cases in which the whole colon is involved, medical treatment almost invariably succeeds.

A simple but valuable test for judging intestinal motility consists in giving a few capsules of charcoal and noting how long it takes the coloring matter to appear in the feces. It takes on an average four and three-eighths hours for the feces to reach the cecum, nine hours to the splenic flexure, and eleven hours to the brim of the pelvis. In defecation all the contents of the bowel beyond the splenic flexure are excreted, so that charcoal given eight hours after the morning stools—say about 4 P.M.—would under normal conditions appear the following morning in the feces, or sixteen hours after its ingestion.

Such a test is useful in diagnosing doubtful cases of stasis.

The feces should be examined in every case of constipation. From the gross examination one is able to make a fair estimate as to the amount of elimination and the general character noted—whether it consist of a formed, well-digested cylinder, or if compressed to the “lead-pencil” shape, as is seen when spasm or stricture exist. When the residue has been retained for a long period of time in the pelvic colon it is apt to be lumpy in character, and

may be streaked with blood derived from the irritation of the rectal mucosa.

The existence of a colitis is characterized by the presence of mucus and, at times, undigested food. The mucus may be mixed with the feces or be passed at the same time, having a viscid, glairy appearance; or else it appears in strings or cylinders—the so-called “bowel casts”—resembling strips of wet tissue paper, which characterizes a mucomembranous colitis.

The significance of such a colitis is, I believe, infection, which may be the result of stasis or, as has been argued by some authorities, among them Keith, of London, the infection being the cause of the stasis, resulting in injury to the intestinal musculature.

The effects of stasis and its resulting toxemia are numerous and manifold.

Much work has been done on the excretion of indican and the ethereal sulphates, and there is no doubt that an excess of indican is often associated with serious intestinal disturbances. But many persons pass large amounts of indican for years and remain in good health, and, on the other hand, indican is not passed in many instances in which the patients might be thought to have alimentary toxemia.

It is generally allowed that the poison is not indol, indican, or ethereal sulphates, but just as we do not know what is the poison in uremia or diabetic coma, so we do not know certainly which are, in every case, the offending microorganisms; nor do we understand the circumstances favoring their appearance and development.

Herter taught that there are probably three groups of cases:

(a) The indolic, in which the probable fault was that of the colon bacillus invading the lower part of the small intestine and the patient was unable to digest carbohydrates and usually passed an abundance of indican.

(b) The saccharobutyric, in which the organism mostly concerned is the *Bacillus aerogenes capsulatus*; the abnormal changes here occur in the large intestine.

(c) A third group composed of groups (a) and (b).

The investigations of Mutch, of London, “on the bacterial activity of the alimentary tract,” have revealed the following facts:

1. The infection of the ileum with coliform organisms is uninfluenced by the gastric secretion.

2. The excretion of the complex tyrosin and tryptophane decomposition products varies directly with the degree of that infection with coliform organisms.

3. The excretion of indoxyl, indolacetic acid, and hydroxyphenylacetic acid is uninfluenced by an infection of the ileum with streptococci or with *Bacillus acidophilus* of Moro, and that hydroxyphenylacetic acid varies in proportion to the degree of ilial stasis.

4. That an infection of the ileum with *Bacillus aminophilus* occurs in constipated persons with subnormal blood-pressure, but not in other constipated patients.

Chronic infection of the ileum with *Staphylococcus citreus* has been shown to be present with chronic septicemia due to the same organism and with the chronic joint, lymphatic, and splenic changes classified as Still's disease.

The constitutional changes and those in the joints, lymphatic glands, and spleen were abolished by colectomy.

Fifty-five ilea of patients without Still's disease were free from *Staphylococcus citreus*.

The above is a brief citation of a portion of the exceedingly interesting work Mutch is doing relative to intestinal chemistry and bacteriology.

The fact remains, however, that whether we have been able to isolate the poison or poisons, or whether such a poison is the result of putrefactive decomposition of stagnant food material, or the result of direct infection of the intestinal tract itself, there has already accumulated a large amount of corroborative evidence to substantiate the fact that under improved intestinal drainage an amelioration or cure takes place in many or all of the symptoms of intestinal toxemia.

It has been constantly argued that thousands of persons are constipated and yet do not suffer from symptoms of poisoning.

When we recall the physiology of the colon it is borne in mind that food enters the cecum through the ileocecal valve in practically a fluid consistency, and that during its passage along the ascending and the first half of the transverse colon the fluids are absorbed, leaving the fecal residue, and that from the distal half of the transverse colon onward there is but comparatively little absorption.

I think it is well substantiated clinically that when the arrest occurs in the descending colon, sigmoid, and rectum it is accompanied by little or no symptoms of poisoning.

I have recently had a patient who suffered from a profound constipation due to adhesions involving the upper portion of the sigmoid; her bowels did not move for periods of four or five days, and then unsatisfactorily after repeated enemata, yet she did not suffer from any symptoms which could be attributed to toxemia. The blood showed, in moderation, the changes generally attributed to constipation, namely, leukopenia, mild anemia, and relative lymphocytosis, but otherwise her general health was comparatively good.

On the other hand, stasis of the cecum and ascending colon is not infrequent with toxic symptoms.

Nature has established certain protective agencies or lines of defence which under physiological conditions prevent the entrance of toxins into the circulation. These are:

1. The healthy intestinal mucous membrane which presents a barrier by its relative impermeability so that their diffusion takes place slowly and time is allowed for the action of the digestive secretions which destroy the microbes and neutralize the poisons.

2. The gastric and pancreatic juices and, to a less degree the bile, all have destructive and neutralizing properties.

3. The liver, which has a high degree of detoxinizing power.

4. The glands of internal secretion.

In undertaking the treatment of any case of constipation the physician must constantly bear in mind that it is a condition into which many factors enter, both psychic and reflex.

There are numerous cases on record which have been treated successfully by the mental healers and the Christian Scientists. Fear, whether conscious or subconscious, is undoubtedly an underlying factor—fear that the bowels will not move. Often a firm assurance that they will move and a discontinuance of the nightly pill are all that is necessary to accomplish the results.

In the past two years we have had a not inconsiderable number of patients who have been treated, so to speak, by “assurance,” with good results.

Of course, in all cases of constipation the education of regular habits in going to the toilet and in not being hurried or interrupted are of the greatest importance.

It is a matter of common experience that exercise is most beneficial to intestinal peristalsis; this is due to both the increase of food intake with its resulting residue and the creating of rapid changes in intra-abdominal pressure, thus, so to speak, massaging the intestines and producing more active peristalsis.

Among the patients who are unable to obtain active outdoor exercise a daily routine of calisthenics may be prescribed. Much help will be found in a practical, well-illustrated monograph by Muller, entitled *My System*.

Massage is of benefit in certain selected cases in which a general state of intestinal inactivity exists, but should not be employed as a routine measure. It should be practised by one who has some knowledge of the general anatomical conditions. Its prolonged or injudicious use may lead to conditions of spasm, and may ultimately prove more detrimental than beneficial. It is contra-indicated in spastic conditions of the colon or when there is any suspicion of appendix disease.

Poorly nourished individuals with the enteroptotic habitus and visceral ptosis, who are almost invariably constipated, require two essentials: the first is an improvement in their general condition and the second a good, firm, well-fitting abdominal support. In these extreme cases of malnutrition nothing short of a thorough rest cure will help their general condition.

Such a rest cure consists of from four to five weeks in bed with

forced feedings, giving them food of high caloric value in small quantities six times a day. The rest in bed removes the drag from the mesentery and allows a straightening out of any tendency to angulation in the intestines.

Fat is first formed in the great omentum, where the blood supply is richest, and such an increase in the omental fat serves as a padding to the prolapsed viscera, giving them a very material support.

By such a "cure" from ten to twenty pounds' weight can be added. Then on allowing them to resume the upright posture—a process which should always be done gradually—a firm, well-fitting support is furnished, which should be adjusted in the morning before getting up and worn through the day. Such a support should be either in the form of a belt or corset. Not only do these supports tend to raise the viscera into a more normal position, but they increase the resistance of the abdominal wall. This resistance is important in raising the intra-abdominal pressure in the act of defecation.

We have had many cases of apparently hopeless invalidism restored to an active, useful life by such procedure.

Diet is an all-important factor in every case of stasis, not alone the character of the food, but the quantity. Some persons, especially those with gastric indigestion, either do not eat enough or else select such articles as leave insufficient residue to stimulate intestinal peristalsis.

To a large degree intestinal activity depends upon the mechanical stimulation of the cellular food residue and the distention of the bowel by food. This distention in its turn is due to the indigestibility of the cellular elements, so that diets lacking in the cellular residue materially diminish peristaltic action.

The chief chemical stimulants of intestinal activity are sugar, organic acids, and their salts. To a less degree are the neutral fats, soaps, and glycerin representing the digestion and bacterial decomposition of meats.

Some authors, among them von Noorden, maintain that the coarse, scratchy diets are suitable in practically all cases of intestinal stasis, even in the presence of mucous or mucomembranous colitis; and that by persisting in them the bowels ultimately become regular and the colitis is cured. Such diets contain practically all the vegetables which are all more or less rich in their cellular elements; especially to be mentioned are oatmeal, whole wheat (not brown) bread, and such fruits as prunes, apricots, etc.

However, when there is a colitis, as evidenced by the presence of mucus in the stools, or when abdominal palpitation shows spasm of the colon, our experience has been that such cases do better on a less scratchy and irritating diet, using such articles as leave less residue, and having them prepared largely in the form of purées.

As the colitis and spasm improve the coarser articles of diet may be gradually added.

The medical treatment of intestinal toxemia is practically purely dietetic, for in no case have we seen more than temporary improvement from the so-called intestinal antiseptics. In certain instances apparently gratifying results are experienced by the lactic acid producing bacilli, but on the discontinuance of their use the old train of symptoms soon recur.

In cases of toxemia one will find the dietetic suggestions of Combes to contain much valuable data. We have used his work largely as a basis for our treatment in auto-intoxication, with good results.

The aim in every case of stasis is to restore the bowel to its normal function, to cut out the use of cathartics, and to correct a faulty hygiene and adopt a diet suitable to the individual case, employing such mechanical measures as are indicated.

There is one preparation, however, which must be considered in relation to these conditions, namely, paraffin oil. The use of this oil was called to the attention of the profession by Lane, of London, and it has deservedly acquired a wide reputation.

There are many cases of stasis in which the circumstances in life prevent carrying out many of the above-mentioned details, where certain anatomical conditions exist that require more aid than we can give by means of diet, supporting belts, and accessories, and yet when we do not feel that the condition is such that an operation is imperative. Paraffin oil, in a large number of these cases, gives most excellent results and, so far as we know, may be used indefinitely and in large amounts. Its results are particularly gratifying in the dry or rectal types of stasis. Some writers have laid stress on the use of a more viscous oil, namely, those of the highest specific gravity; but in our experience this has not been a very important point and the lighter oils have given equally good results.

Some patients complain that the oil oozes from the anus or will be passed without producing any movement. This can sometimes be avoided by the use of a little agar-agar in conjunction with it. As a rule, after a few days and when the fecal stream has been started the leaking ceases. Agar-agar is a simple carbohydrate from seaweed. It has the property of absorbing water and resists the action of intestinal enzymes and bacteria; it passes practically unaltered through the intestines, increasing the intestinal residue, but in itself is not particularly efficacious. It should not be used in cases in which there is any evidence of an inflamed intestinal mucous membrane.

In the majority of cases of beginning treatment for stasis it will be found necessary at first to move the bowels every second or third day either by the use of saline or oil enemata. Such a course

of enemata will in itself clear out an impacted rectum and often start the bowels working in a normal manner.

No paper on the subject of stasis and intestinal toxemia is complete without the mention of autogenous vaccines. Within the past two or three years some sporadic work has been done along these lines with varying degrees of success; for the past two years we have been using such vaccines, having cultures made from the stool and taking out the predominating organism, which generally consists of the colon bacilli.

In many instances vaccines used in conjunction with diets and general hygienic measures have given us most excellent results, the symptoms of toxemia clearing up; and in some cases the bowels have taken on a normal function with little or no further treatment. We feel that in the more pronounced cases of toxemia they are certainly worthy of a trial.

Organotherapy, although still in an empirical stage, infrequently gives some brilliant results in stimulating the insufficient antitoxic function of the organs of internal secretion. Thyroid extract administered in grain doses after meals in many cases of long-standing toxemia helps the overworked internal secretions in their efforts to neutralize the poison.

Our endeavor has been, in a limited time, to make a brief outline sketch of the present-day conception of stasis and its medical treatment, together with its complication, intestinal toxemia.

The surgical aspect of the subject will be discussed by Dr. McWilliams.

#### SURGICAL CONSIDERATIONS BY DR. MCWILLIAMS.

The surgical treatment of constipation and intestinal stasis is probably the most frequent and prominent topic before the medical world today. Scarcely a medical journal appears without an essay on intestinal stasis. Notwithstanding the discussion and experimentation that is being conducted, the proper surgical treatment of the condition will eventually be worked out on a rational basis, and it will find its proper place as other procedure in surgery have done in the past. In the mild and non-toxic cases, it cannot be too strongly emphasized that thorough medical measures should be persistently conducted before thinking of resorting to surgery. In the severer toxic cases it is well to have a thorough Roentgen-ray examination of the intestinal tract made at the outset of the treatment, so as to rule out the presence of any gross surgical lesion in order that valuable time may not be lost in unavailing medical treatment when the patient may need surgery. Surgery is a valuable succedaneum to medical treatment when it is used with intelligence and judgment. We take issue with those who advocate the removal of the large bowel for two

main reasons: (1) because of the immediate high mortality of the operation, which is between 30 and 40 per cent., an altogether too great mortality; it seems to us, to warrant the surgeon in performing it for a malady which, in the vast majority of cases, is not in itself fatal, and (2) because the removal of the entire large bowel is at times followed by an intractable and exhausting diarrhea which may last for months. At the present time the writers know of a patient whose entire colon was removed for intestinal stasis three months ago in one of our large institutions. Her condition has been and is now most pathetic, for she has been in bed since the operation, having from twenty-five to thirty loose stools a day, and these cannot be controlled. Lane says these cases of diarrhea after operation will eventually clear up; but what opprobrium is brought upon surgery when an operation is done which may lead to such an unfortunate result—worse than the lesion for which the operation was performed.

The short-circuiting operations, such as placing the terminal ileum in the sigmoid flexure or rectum, have a low mortality, but, as a rule, they have failed to cure because of a backing up of the feces into the excluded gut, where they remain, allowing absorption to take place from them. Distressing diarrhea may also occur after this operation. The operation has, however, seemed to do good in some selected cases, and may be tried, but the surgeon should not be disappointed in not effecting a cure. It would seem as though this operation could do the patient no great harm other than a more or less transitory diarrhea.

An operative procedure which, we believe, will be found to be the best in those severe cases in which no other surgical lesion can be discovered to account for the stasis, is the removal of the cecum, ascending colon, hepatic flexure, and half of the transverse colon. In this operation the immediate mortality is lower than in total colectomy, and the remaining portion of the large bowel will allow of a solidification of the feces, so that there will be no subsequent diarrhea, or if there be any, it will be but slight and transitory. The ends of the ileum and the transverse colon may be closed and a side-to-side anastomosis made between them, or if speed be advisable a Murphy button may be placed between the end of the ileum and the side of the transverse colon, the end of the colon being previously closed.

Before resorting to this radical procedure, however, a thorough exploration should be performed to endeavor to find some surgical lesion which may be removed by less severe measures. A right rectus incision should be made, beginning at the navel and running up as far as necessary. The incision is made close to the inner border of the rectus muscle, which is retracted outward. The gall-bladder is first explored for calculi and for adhesions to the duodenum and transverse colon. Our feeling is that if it can be done



without undue risk to the patient the gall-bladder, if it is adherent or is pathological, should be removed, as this will be the best guarantee against a recurrence of the adhesions and inflammation. Gastric and duodenal ulcers should be next searched for and, in the ordinary case, if they be present all that will be necessary will be a gastro-enterostomy, to which may possibly be added the closure of the pylorus by wrapping around it a strip of fascia, best taken from the rectus aponeurosis.

The various mechanical causes of intestinal stasis should then be searched for and, in order to understand exactly what we are to search for, it will be necessary to give a brief *résumé* of these causes. It is only when the contents of the large intestine stagnate unduly that harm results, and the more the stagnation in the large intestine, the greater is the resultant harm. The worst cases are those in which prolonged stasis occurs both in the large and in the small intestine. Stasis in the lower end of the ileum is produced in three ways: First, the simplest of these is for the appendix to be so placed that it interferes with the passage of the ileal contents into the cecum when the patient is upright. The appendix is then usually internal, retrocecal, and its tip firmly attached high up, allowing the proximal and distal loops to sag, while the portion of the bowel attached to the appendix remains fixed, producing obstruction. A second means of obstruction is the following: any marked degree of stasis in the large intestine will lead to delay in the passage of the ileal contents into the cecum, which is already overfilled. The loaded ileal coils consequently drop into the pelvis and the terminal coil of the ileum rises vertically over the pelvic brim to the ileocecal entrance, and the ileal contents are therefore compelled to ascend a long vertical path, the prominence formed by the pelvic brim and the sacral promontory producing more or less obstruction. In some patients the cecum also occupies the pelvis, and it may become abnormally elongated, dilated, and mobile. A third way in which ileal stasis is produced is by Lane's ileal band, which is caused by the continued pull on the mesentery by the overloaded ileum, resulting in the formation of thickened bands in the situations where the pull is the greatest. These bands tend to prevent the dropping of the ileal coils; that is, some of the coils drop while others remain fixed. In general enteroptosis, if all the coils prolapse equally there may be no difficulty in defecation. It is the irregularity in the position of the prolapse which in other cases produces the difficulty. A single band, Lane's ileal band, placed within four inches of the end of the ileum is most potent to produce obstruction in the subjects with ileal stasis. With this band, while the patients are recumbent, no obstruction exists. This is the reason why recumbency in bed, the importance of which Dr. Barclay has dwelt upon, is so helpful. In the upright posture, however, the cecum drops on one side of the fixed band

while the ileum prolapses on the other side. The bowel is consequently held up at the kink and its lumen is obstructed at this point. The results of these three methods of producing obstruction are the same. Bacteria invade the stagnant ileum from the cecum and ascend the small intestine, where their influence is exerted the most severely at the upper end, as on the duodenum, causing ulcers; on the gall-bladder, producing inflammations and calculi; and on the pancreas, causing chronic pancreatitis. Jordan says that in operations on the subjects of ileal stasis the duodenum, which is fixed, is always found to be distended, due to the kink producing obstruction at the junction of the fixed duodenum with the free jejunum, produced by the jejunum being pulled vertically downward by the overloaded lower ileal coils.

**Stasis in the Large Bowel.** The cecum tends to become dilated, elongated, and displaced into the true pelvis, which it occupies to the inconvenience of other structures. This tendency to fall is met by new bands being formed, external to the cecum and ascending colon, which fix these structures to the abdominal wall (Jackson's membrane). The lowest band includes the appendix and may produce symptoms of varying severity comprised under the term of "chronic appendicitis." The next kinks which develop are those at the hepatic and splenic flexures. These are very rare. To meet the drag caused by the prolapsed transverse colon in addition to the loaded cecum, peritoneal bands develop which drag these flexures upward and convert the passage from a round turn into a sharp kink. This is exaggerated still further by the formation of bands connecting the adjacent surfaces of the prolapsed transverse colon with the sides of the ascending and descending colons, which serve to transmit some of the weight of the loaded transverse colon through the ascending and descending colons to the abdominal wall, thus taking off some of the strain from the convexity of the stomach. These bands are evolutionary and are not inflammatory. The transverse colon may sag so like a V that its apex may come to occupy the pelvis, where it may become adherent.

By the kinking at the hepatic and splenic flexures, obstruction may rarely be produced. A kink may develop at the level of the iliac crest on the right side, where a strong band of adhesions may attach and control the lumen of the ascending colon sufficiently to cause some obstruction at this point. Another band may develop between the under surface of the liver and gall-bladder and the pylorus and transverse colon, producing obstruction. The "last kink" affects the large bowel on the left side where it crosses the brim of the true pelvis. These latter bands develop early in life and form between the peritoneum of the iliac fossa and the outer surface of the mesentery. The ovary and Fallopian tube are often involved in these adhesions.

We will now continue the exploration of the abdomen, which was interrupted above. Adhesions binding the transverse colon and pylorus to the liver and gall-bladder should be divided transversely. The operative treatment of duodenal distention, due to kinking at the duodenojejunal junction, resolves itself into the removal of the obstruction at the lower end of the ileus, and consists in the transverse division of the controlling band, *i. e.*, Lane's ileal band, with vertical suture of it and in the removal of the appendix. An elongated, dilated, mobile, prolapsed cecum may be latterly plicated after removal of the appendix. That is, two of the vertical striae are sutured transversely together by a continuous silk suture, or even more of the diameter than this may be infolded, and the cecum may then finally be sewed fast to the iliac fossa, "Jackson's membrane," binding the outside of the cecum to the abdominal wall, should be divided and sutured. A long, V-shaped, transverse colon, which is adherent in the pelvis, should be freed and lifted up. Adhesions binding its sides to ascending and descending colons should be divided and the transverse colon may be secured in its place, if thought advisable, by Coffey's suspensory operation. In this procedure the gastrocolic omentum is sutured widely to the anterior abdominal wall. This not only supports the ptosed transverse colon, but also the stomach, or, what is perhaps better, the great omentum below the transverse colon, with the gastrocolic omentum above, the transverse colon may together be sutured to the anterior abdominal wall. This elevation of the transverse colon will do away with any possible kinking at the hepatic and splenic flexures. Any band kinking the sigmoid should be divided.

Such in brief outline are the surgical procedures which may be done in cases of intestinal stasis when surgery is needed. We may say, however, in conclusion, that in the majority of cases, provided there be no congenital defect present, the conditions producing intestinal stasis are preventable and should not be allowed to develop into the stage where operative intervention is necessary. A more intelligent appreciation of the importance of exercise, diet, proper hygiene, of the position of the viscera, and of adequate support of the abdominal organs will go a long way toward preventing the stasis of large amounts of material at given points in the intestine. With this accomplished the development of chronic intestinal stasis will be forestalled. If after prolonged study by a competent medical man who has a proper appreciation of the physiology of the abdominal organs, supported by good Roentgen-ray pictures, it seems wisest to operate, in the event of failure of thorough medical treatment, the great question confronting the surgeon is to know what surgical principles to carry out and how much to do. The one thing which surgeons seem agreed upon that is proper and allowable to do is this, namely, to divide any adventitious bands,

which the Roentgen-ray pictures indicate are causing obstruction, and to remove the appendix. Further procedures bring the surgeon upon debatable ground. Opinions and statistics differ so upon the value of the various visceral supporting operations that a conservative surgeon with our present knowledge will hesitate before adopting most of them. Except in very exceptional cases the short-circuiting procedures should be avoided, while the removal of the whole large intestine, in our opinion, should never be done for intestinal stasis alone. In the severest and worst cases a safer operation is the removal of the cecum, ascending colon, hepatic flexure, and half of the transverse colon. In any case, both before and after any operative procedure, a well-fitting, efficient, supporting apparatus should be worn and medical measures persisted in, particularly the use of Russian oil in gradually decreasing doses. Wilson<sup>1</sup> says: "It is interesting to observe Lund's<sup>2</sup> convincing conclusions that cures will be rare after operation for visceroptosis. The adverse reports that are rapidly accumulating are convincing that visceroptosis is not always cured by operation and that there must arise some skepticism when an overenthusiastic operator reports brilliant results that no one else can see or obtain."

This paper has not dwelt upon infections of the large bowel, but when this is present, resisting all medical treatment, a better procedure, and one more efficacious than an appendicostomy is an ileostomy or opening in the lowest portion of the small intestine, which will assure absolute rest for the bowel below the opening.

## THE WASSERMANN REACTION IN PREGNANCY.<sup>1</sup>

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THE serum diagnosis of syphilis has in no department of practice proved of more value than in that of obstetrics, involving, as it may, two patients at the same time. Further, the routine examination of all antepartums for the Wassermann test, wherever possible, is strongly urged as latent syphilis may be shown in no other way.

<sup>1</sup> Med. Rec., April 17, 1915, p. 775.

<sup>2</sup> The Surgeon and the Ptois Problem.

<sup>3</sup> This paper was read before the Hospital Graduates' Club of Brooklyn at a stated meeting, and the Plainfield Clinical Society. A few additions have been made to the paper since that time, consisting of a larger number of examinations, but our conclusions have been practically the same.

For some time this has been carried out at the Kings County Hospital, and, more recently, at the writer's suggestion, the routine examination of fetal serum as obtained from the severed umbilical cord at birth, both procedures with the happiest though not always conclusive results. We have still to learn much concerning the Wassermann reaction, especially from the standpoint of treatment, dosage, pregnancy, time of administration, contra-indications, etc.

The percentage of positive reactions varies with the period of the disease, and whether the infection is acute or latent, hence primary cases where the lesion is present less than two weeks usually show negative, while if the sore is present over four weeks, 75 per cent. positive is found. Secondary syphilis, with symptoms, gives positive in 90 per cent. and tertiary in 75 per cent. Syphilis without symptoms (latent) shows in the untreated cases, 75 per cent. in early cases, and about the same (76 per cent.) in the late ones. The few other diseases showing positive Wassermans are not likely to be confused with syphilis, or can be readily excluded, such as pneumonia, which is said to give positive for a few days following the crisis; malaria giving 20 per cent. positive in cases with fever and untreated; the tubercular type of leprosy showing positive in a large percentage of cases; and yaws, which gives as high a proportion of positive as syphilis.

The test was made 892 times in our wards, of which 821 were negative and 71 were positive (7.9 per cent.). A considerable number, not included, were admitted in labor and the blood not examined, though we are now having these taken as well, postpartum. A majority of the positive patients examined had no visible lesions, and would have been overlooked but for the routine Wassermann.

The treatment varied from "606" to mercury by inunction and hypodermics. Those who received no treatment before delivery either refused it or were admitted in labor, and one case was overlooked inadvertently. Those admitted in labor whose Wassermans were positive postpartum received treatment before discharge in the majority of cases. We are not as yet able to control the treatment of syphilis in pregnant women when they are admitted to the hospital for some cause other than pregnancy, but we expect eventually to do so, at which time every pregnant woman with syphilis, whatever the period of gestation and in the absence of contra-indications in the kidneys and eyes, will receive "606." We do not share the fear expressed by some of giving "606" in late pregnancy.

One case admitted in labor had been given salicylate of mercury by hypodermic injection intermittently before admission, with no effect on the lesions, and she presented some beautiful specimens of rupia in addition to a 4+ Wassermann; the child was saved, however, by the treatment and had a negative blood report, though

a rash developing a few days later was pronounced probably specific by the dermatologists. Of the living children (277 examinations) all were born without lesions and but 12 of the 277 had a positive Wassermann. A few were not examined for this reaction, as that was not a part of the routine at the time of their birth.

One of the babes with a minus Wassermann was admitted to the Children's Hospital a few months later in a moribund state with a diagnosis of marasmus. Examination of the blood and spinal fluid proved a 4+ Wassermann.

Another woman had a very interesting history: Her first blood examination was 4+ on April 10, 1913; "606" given April 27; 4+ on May 15, 1913; "606" given May 27, and June 19, 1913, and no further treatment given. Later examination, on October 16, was 4+, and she delivered a dead and macerated fetus on October 28, 1913.

The history of miscarriages was of doubtful value, a majority of the positive cases recording that accident one or more times, while the remainder were either primigravida or had borne living children, with no miscarriages. Few of the series of miscarriages had histories pointing definitely to syphilis as a cause. One had a live child four and a half years ago, alive and well today; then occurred four premature labors, all at or about the seventh month, for the last of which she entered our service in labor in March, 1913, following which she has had a 4+ Wassermann. She left without treatment. Seen some time afterward she was again pregnant, had reached the sixth month with a live child, and her blood was still 4+ without any treatment. She entered our service at once for treatment and the outcome was awaited with interest. This patient received numerous injections of mercury salicylate, both before and after entrance to the hospital, none of which was given until after the sixth month. While they did not affect her reaction, being 4+ at the time of delivery, she delivered herself of a live child, weighing 9 pounds 10 ounces, without visible lesions and with a negative Wassermann. This child, however, became ill at the end of one month, was admitted to the children's service of the Kings County Hospital as a syphilitic, and died of syphilis at the end of the third month.

Another case had a live child in 1909 which died at the fifth week, she states, of an infected cord, one miscarriage at the fifth month in 1910, and another at the third month in 1911. She had a live child in October, 1913, without any treatment, but the child's blood showed a 4+ Wassermann at birth, and it developed a rash a few days after birth, which, while the dermatologists were unwilling to call it syphilitic, cleared up after mercury was placed under the baby's binder. The mother's Wassermann varied from a very doubtful positive on the first examination to three decided negatives on subsequent tests.

Baily, quoting Bat and Daumay, considers that a solitary negative in pregnancy does not mean surely that syphilis is absent, but one positive is evidence of certain maternal and probable fetal infection, and indicates the necessity of active treatment. They find when infection has occurred sometime after conception there is a higher percentage of positive results with the mother than with the infant.

Treatment of the mother during pregnancy gives a negative reaction in the infant, but one negative does not necessarily mean that the infant is all right and can be suckled by a healthy wet-nurse, as syphilis may be latent. Of 35 mothers whose babes showed signs of syphilis, 26 gave a positive and 9 a negative reaction. The large majority of cases with positive at birth, later develop symptoms of syphilis, and the large majority of cases negative at birth remain healthy.

Examination of the maternal blood shows:

1. The mother may be positive and the child minus. (A majority of our cases were such.)
2. The mother may be minus and the child positive. (A few of ours agreed.)
3. The mother may be positive and the child positive. (Ours agreed only in untreated cases.)
4. The mother may be minus and the child minus. (As would be expected, there our records coincide.)
5. The mother may be doubtful and the child positive. (We now have such a case under observation.)

Probably one need have little fear for the child if the mother is negative. Of congenital syphilis it may be said that practically all infants or children showing symptoms give positive reactions, but not all children born of syphilitic mothers; while of living children born of syphilitic mothers nearly 50 per cent. give a negative. Our percentage for such cases was even higher, owing to the mother having had treatment.

The precaution must be observed, however, that if the child has been delivered after an anesthetic has been given to the mother the blood of either the mother or child be not examined for a full twenty-four hours after delivery, as the results may be erroneous. The same holds true regarding the ingestion of alcohol by the mother.

Boas examined the reaction in 44 infants, who showed either syphilitic lesions or were born of syphilitic mothers, and his results were: 20 positive and 24 negative. 20 positive: 16 had symptoms at birth or within three months, 4 had no symptoms in three months, and the reaction became negative rapidly. 24 minus: 17 remained negative and had no symptoms; 5 developed symptoms and positive reactions; 2 died with negative and yet proved to be syphilis.

Antisyphilitic treatment during pregnancy can result in the birth of healthy children and such children are free from syphilis and may be quite healthy or show various positive defects. Latent syphilis

(positive reaction without symptoms) is common in early years, explaining Profeta's law, immunity of the healthy children of specific mothers. The immunity of the child in Profeta's law and of the mother in Colles's law is only apparent; they cannot contract the disease because they already have it in latent form.

Miller<sup>2</sup> states: "The Wassermann has been positive in practically all forms of congenital malformations." In addition there should be included the cases of so-called marasmus, more properly infantile atrophy.

One of the most marked tendencies of babies born of mothers late in the maternal disease is that to hemorrhage and jaundice. We use whole blood in these cases in our service at the Kings County Hospital with great success.

An intermittent fever in the later months of pregnancy has been pointed out by Taussig,<sup>3</sup> of St. Louis, as being often of syphilitic origin.

The further development of luetin by Noguchi will place in the hands of the general practitioner a method of diagnosis easily used by himself and within reach of the ordinary patient's purse. We must realize that the fee for caring for obstetric cases is so small that the practitioner cannot afford to have any portion of it taken away from him by the laboratory man.

The treatment of syphilis during pregnancy is the same as at any other time.

The author differs in his opinion from those who state that the existence of a pregnancy is a contra-indication to the use of salvarsan and adopts the attitude of von Zeisl, who states that because of the rapidity of its action, it seems especially suited to syphilitic pregnant women with a view to the prevention of abortion and the delivery of a sound child.

I wish to thank my associate, Dr. William Pfeiffer, for his assistance in compiling these records.

## THE CRANIAL DEFORMITY OF OXYCEPHALY; ITS OPERATIVE TREATMENT, WITH A REPORT OF CASES.

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DURING recent years, much interest has been aroused in the relation of cranial deformities to optic nerve atrophy; Patry has stated that almost all cranial deformities occurring in the

<sup>2</sup> Cleveland Med. Jour., July, 1912.

<sup>3</sup> Surg., Gynec. and Obst., July, 1910.



first five years of life result in optic nerve atrophy. In 1873 Michel was the first to observe the frequency of optic nerve atrophy in cases of cranial deformity, and this is especially true of those cases of cranial deformity known as the "turmschädel" variety—meaning merely tall heads or high skulls; this is particularly true of the extreme type of the turmschädel skull—the oxycephalic type which is not merely a tall head but one with a prominence or protrusion at the anterior fontanelle.

NAMES. Much confusion has arisen in the literature of this subject due to the variety of names that have been used to designate this cranial malformation; among those names frequently observed are "turritum caput" (Welker); "tete a la thersite" (Hamy); "acrocephalie" (Lucæ); "spitzkopf" and "hypsiccephaly" (Oliver). These names are used in describing abnormally tall heads whether of the frontal or occipital type. The two names which have been used most frequently and interchangeably are turmschädel and oxycephaly, and it seems wiser to consider the two names as applying to one condition which differs only in the degree of the deformity, "turmschädel" or "steeple-shaped skull" for the mild form of the condition, where there is no definite prominence or protrusion at the anterior fontanelle, and "oxycephaly" for the more severe cases with a prominence at the anterior fontanelle.

Most of the observations of this condition have been made by oculists, since the patients have been brought to them on account of the failing eyesight and nystagmus; very frequently the cranial deformity has been overlooked. Von Graefe reported the first case in 1866 in a male child, eight years of age, whose head was very high but narrow transversely; there had been a gradual onset of blindness which proved upon ophthalmoscopic examination to be due to a "symmetrische neuroretinitis"—the picture of a typical choked disk. This case apparently was one of mild degree—the turmschädel type. Since then many cases have been reported—about 80 in all—the vast majority of which have been of the turmschädel type, merely tall heads with optic nerve atrophy of varying degrees; unless there is visual impairment, the cranial deformity is rarely considered important enough to warrant a doctor's opinion and therefore very few such cases have been carefully examined; such cranial deformities however, must be very mild, for slight cranial malformations, especially of the turmschädel variety, do produce ocular disturbances in varying degrees—the greater the deformity, the greater the eye disturbance. Hanotte has stated that practically all of the so-called "oxycephalic" heads in the "Ecole d'Anthropologie" (Catacombs), and in the "Gallerie d'Anthropologie du Museum" are merely tall heads with no protrusion at bregma, being similar to the skull of Sir Walter Scott. However, if eye disturbances were produced by such tall heads, they should undoubtedly be classified as mild types of the turmschädel

variety of cranial deformities. Not more than 20 typical cases of oxycephaly have been reported, that is, cases of the severe turmschädel variety of cranial deformity with a prominence or protrusion at the anterior fontanelle; all of these cases produced optic atrophy of varying degrees.

ETIOLOGY. Many theories have been formed to account both for the cranial deformity and its closely related optic atrophy. Most observers are now agreed that a premature synostosis of the occipital, parietal and the temporal bones has allowed the brain to grow and expand only in the direction of the anterior part of the skull, producing either the high turmschädel type of skull, or in severe cases and more rarely the enlargement and bulging prominence at the anterior fontanelle of the oxycephalic skulls; the resulting increase in the intracranial pressure gradually producing a secondary optic atrophy, very similar to the effect of a brain tumor, which as it grows, slowly raises the intracranial pressure and so produces a typical choked disk, and if prolonged, a secondary optic atrophy. It was formerly believed, especially by Manz, Ponfick and others, that a narrowing of the optic foramina was caused by an osteitis, forming hyperostoses which compressed the optic nerve and in this way a primary atrophy resulted, as well as the other cranial deformities; such a view, however, has not been confirmed by autopsies by Vortisch, Weiss, and Brugger except in 1 case reported by Ponfick and 1 by Michel.

Bertolotti firmly believes that rachitic craniotabes and oxycephaly belong to the same rachitic process, and only after the synostosis of the sutures of the skull does the picture change and oxycephaly individualize itself. But what is the exciting cause for the premature synostosis of the sutures of the skull? Very many opposing views are held; Virchow, Vortisch, Hirschberg, and others believe that the premature synostosis is due to a fetal hyperemia and inflammation of the meninges due to inherited syphilis, nervous instability from alcohol, epilepsy, and the result of difficult labors. Bertolotti, Meltzer, Obermuth and others are convinced that the underlying cause is rickets—as Bertolotti says, it is a “dystrophy of rachitic origin,” whereby mild meningitis causes a slight inflammation of the sutures of the skull and hence stimulates the genetic growth of these bones; in this manner the sutures become closed prematurely, especially in the posterior portion of the skull, and as the gradually increasing intracranial pressure can only expand in the anterior part of the skull, the deformity of turmschädel and oxycephaly results. Bertolotti states that in 85 per cent. of his cases there are skeletal evidences of rickets; the report by Meltzer in his review of 20 cases is the same.

Such, however, is not the view of many other observers, such as Fletcher, Enslin, Dorfman and others, who believe that the condition is due to some underlying cause the nature of which at

present remains obscure; it is not believed to result from an early meningitis in that the cranial nerves are not affected, nor is there a marked mental defect; in fact, the cases are all unusually bright and intelligent; nor have there been any cases reported which at autopsy disclosed a hydrocephalus or even any signs of a previous meningitis. The theory of its being a "dystrophy of rachitic origin" is very strongly opposed by the fact that in cases suffering from rickets the closure of the sutures is delayed (not premature) and the deformity of the head is different; besides, few cases have been reported which have disclosed definite skeletal signs of rickets, such as enlarged radial epiphyses, rosary, etc.; Oberwarth however, states that 5 of his 7 cases showed definite signs of the "Englische-krankheit." In the 4 cases reported here no such signs were to be found, nor were they to be found in any of the cases reported by Enslin, Carpenter, Hirschberg, Stephenson, Fletcher, Dorfman, Dodd and McMullen and others.

There seems to be no predisposing factor in producing this condition. No race is exempt apparently; about an equal number of blondes and brunettes have been reported. It is far more common in males than in females, the proportion being about 5 to 1; of 17 cases of *turnschädel* reported up to 1893, 15 were males and only 2 were females (Friedenwald). Of the 7 cases each of Videcky and Hirschberg, 6 were males; of the 8 cases of Oberwarth, 6 were males. Heredity has little or no effect, the family history usually being very good and the other children of the family being in excellent health. Hirschberg reports 1 case where the maternal grandfather was an oxycephalic; Weiss and Brugger mention 2 oxycephalic brothers seen by Oeller, and Hanotte states that Hamy observed 2 oxycephalic sisters; Carpenter also reports the cases of 2 oxycephalic sisters. Apparently syphilis is not a factor, nor is traumatism.

The intelligence is unimpaired, the patients being unusually bright and intelligent. If mentally backward it is usually due to loss of eyesight, *i. e.*, "deprivation" (Ireland), or to the gradual deterioration of epilepsy. Practically all of the cases of Meltzer, Groenouw, Fletcher, Enslin, Friedenwald, Hirschberg, and Oberwarth have been normal mentally.

Among the possible mild types of *turnschädel*, such as abnormally tall heads, Patry cites the examples of the skulls of Sir Walter Scott, Paracelus, William Humboldt, Mechel and others who were exceptionally intelligent men.

COURSE. There are three main groups of *turnschädel* cases classified by Fletcher according to the date of the onset.

1. When the cranial deformity with possible optic atrophy was present at birth—the congenital cases; these are comparatively few in number.

2. When the cranial deformity and possibly "large eyes" are

observed during the early months of life or during the first two years; this deformity and impairment of vision are gradually increased.

3. When the earliest signs are noticeable for the first time between the second and sixth years of life, usually some visual impairment, associated with headaches and occasionally with "fits." This group includes the majority of cases, and it has frequently been observed that the cranial deformity becomes much worse and the headaches and "fits" more severe as the impairment of vision progresses and the resulting blindness occurs. The duration of life is not shortened in many mild cases, though it is very exceptional to hear of cases after fifty years of age; Hirschberg and Grunmach believe that very few cases of average severity survive puberty.

Regarding *turnschädel* as the mild form of oxycephaly, both being due to the same cause with only a difference in the degree of severity, let us consider then its characteristics, remembering that in oxycephalic cases there is a bony prominence at the site of the anterior fontanelle.

SIGNS. There are really three cardinal signs of the *turnschädel* type of cranial deformity, namely:

1. The type of cranial deformity.
2. Exophthalmos with divergent strabismus.
3. Impairment of vision.

1. The cranial deformity.

(a) This is characterized by the great height of the forehead which towers over the face.

(b) Feebly marked supraciliary ridges.

(c) Temporal ridges and depressions are feebly marked.

(d) A possible "*crista sagittalis*," a more or less prominent ridge along the sagittal suture anteriorly.

(e) Very high shallow orbits, the roof of the orbit being almost perpendicular and its depth being far below normal. Bertolotti's orbital index is 94 to 110 (normal 85 to 88); that is, the vertical diameter being equal or greater than the transverse diameter.

(f) Nasal septum deviated to one side.

(g) Hard palate sharply arched, narrow and frequently asymmetrical.

(h) Face may be asymmetrical, due usually to a flattening or depression in the malar and supramaxillary region.

(i) The Roentgen-ray picture is very characteristic. Much importance has been laid upon the profile of the base of the skull by Bertolotti; the *turnschädel* type shows a "*lordose basillaire*" and not a "*cyphose basillaire*," as is shown in *dysostose-eleido-cranienne* and in *hydrocephalus*. The middle fossa is almost upon the same level with the posterior fossa, while the sella turcica is much widened and deepened. The head sinuses are practically obliterated particularly the frontal and the ethmoidal sinuses, while there is only a trace of the sphenoidal and mastoid cells.

The great wings of the sphenoid are flattened out and are not so vertical. Whereas the anterior projection of the opisthionbasilar line strikes 4 to 5 cm. above nasion in dysostose-cleido-cranienne and hydrocephalus, yet in the turmschädel type of deformity it strikes below nasion. The facial angle is increased from 8 to 10 degrees above the normal 54 degrees of Cuvier, though the increase is due more to the shortening of the inferior maxilla and the general "adenoid expression" of the patient, practically all of the cases being mouth-breathers.

An interesting observation is the remarkable thinning of the bones of the cranial vault and the formation of the "digital impressions" or holes on their inner surface—due undoubtedly to the pressure of the underlying convolutions. In the severe form of the turmschädel type of skull, the oxycephalic type, there is a characteristic bulging at the anterior fontanelle, usually covered by a thin layer of bone; it may be as large as a lemon, but in the majority of cases it is noticeable only upon careful observation. In all such cases of oxycephaly the "crista sagittalis" is always present. In some cases the thinning of the occipital bone advances so far as to produce an opening at the site of the external occipital protuberance, so that a definite pulsation and venous thrill can be distinctly palpated.

2. The exophthalmos with divergent strabismus and nystagmus is present in varying degrees in practically all well-marked cases; the patient may be unable to close his eyes. This exophthalmos is undoubtedly due to the very shallow orbits; Weiss and Brugger measured four turmschädel skulls which showed an orbital depth of 10 mm. less than the normal depth and 6 cm. less than the normal orbital contents. This abnormality is caused by the great wings of the sphenoid being posteriorly placed instead of externally, and by the vertical position of the roof of the orbit.

Very rarely is the strabismus convergent. The divergent strabismus is frequently unequal, the left eye being usually the more extreme.

Nystagmus is very common; it is usually bilateral and in all directions. Of the 20 cases of mild turmschädel reported by Meltzer, exophthalmos was present in 18, divergent strabismus in 19, and nystagmus in 19.

3. The impairment of vision is always the result of a secondary optic atrophy of varying degrees; it is present in practically all cases. The younger the case the better the vision, unless there is a complete optic atrophy at birth. The ability to read is rare in adults. One eye may have a contracted visual field, and the other eye be completely blind. Unless there is a total amaurosis the two eyes rarely show the same degree of optic atrophy. The picture of the beginning optic atrophy is one always seen in the later stages of brain tumor where the increased intracranial pressure has first

produced a "choked disk," and then its subsequent secondary optic nerve atrophy. This impairment of vision is usually noticed between the second and sixth years of life, progresses to a certain degree, and then stops—whether blind or not. It never produces blindness in adults.

As stated above, many theories have been used to account for this optic nerve atrophy, but it is now generally believed to be the result of the increased intracranial pressure, typical secondary optic atrophy from pressure and not a "postneuritic" condition resulting from inflammation, etc. It is most rare for the optic atrophy to be a primary one.

The loss of smell is rather frequent; Meltzer reports 12 in 20 cases. Hearing has been dulled in a number of cases. Occasionally the sense of taste is lost.

Other malformations frequently associated with cases of turn-schädel deformity are:

1. Webbing of the fingers and toes (Carpenter).
2. Malformation of ears and fingers.
3. Unduly prominent internal condyle of humerus which deflects the forearm outward and may prevent complete extension (Fletcher).

4. Of 20 cases reported by Meltzer, 14 had narrow and deformed noses, while 5 had adenoid growths. Carpenter has reported the cases of two sisters (two and four years, respectively, and typically oxycephalic) who had:

1. A systolic cardiac murmur.
2. Webbed fingers, same type in each.
3. Six toes on each foot and fewer number of phalangeal joints—only two as a rule.

4. Hernia. One sister had both an umbilical and an epigastric hernia, while the other one had an umbilical hernia.

**SYMPTOMS.** The most constant symptom of this type of cranial deformity is severe headache, usually limited to the frontal and occipital regions. The child will bury its head in the pillow, holding it with both hands, and will cry almost continuously. The headache is most severe when the eyesight is rapidly failing, *i. e.*, during the time when the intracranial pressure is greatest.

Very frequently the protrusion at the anterior fontanelle and the general deformity of the head are now noticed for the first time. As the child grows older the headache may disappear entirely. It is at this early period that convulsions are likely to appear for the first time, and as the eyesight fails the "fits" become more frequent; rarely do the convulsions become chronic unless the epileptic "habit" is acquired.

**TREATMENT.** The treatment of this condition has been most unsatisfactory. A palliative expectant treatment has been followed in the cases which have been recognized as being cases of oxycephaly.

A symptomatic treatment in no way retarded the advance of the condition; the increased intracranial pressure gradually produces a secondary optic atrophy and thus blindness results; the headaches may be most severe.

Until recently no attempts have been made to relieve this intracranial pressure and thus avoid its harmful effects. This neglect has been due apparently to a misunderstanding regarding the cause of the optic atrophy, the factor of intracranial pressure having been overlooked. Some years ago von Eiselsberg trephined a case, but all trace of the patient was lost shortly after the operation. In 1911 Cushing performed four operations upon one case of oxycephaly to elevate the entire top of the head in order to lessen the increased intracranial pressure; not only were these operations quite formidable, but there was a marked tendency for the cut edges of the vault to fuse rather closely, thus tending to obviate the benefits of a permanent relief of the intracranial pressure.

It then occurred to me that the increase of intracranial pressure in cases of oxycephaly might be lessened sufficiently by a single, and if necessary a bilateral, subtemporal decompression; in early cases the operation might prevent the onset of a secondary optic atrophy and possibly produce such a lessening of symptoms and signs that a normal child would be obtained.

My first case of oxycephaly was operated upon by me at the Johns Hopkins Hospital, September 15, 1911, and has become a normal child apparently. The second case was operated upon by me at St. Luke's Hospital, Shanghai, China, March 8, 1912; all trace of this child was lost shortly after the operation. My third case of oxycephaly was operated upon at the Polyclinic Hospital, New York City, April 28, 1914; this child made an excellent recovery, becoming more and more normal. My last case was an extreme type of oxycephalic deformity, and has shown a marked improvement since the operation March 15, 1915.

I offer these cases with their operative treatment in the belief that an early relief of the intracranial pressure in cases of oxycephaly will prevent the harmful effects of such pressure—headache, secondary optic atrophy with the resulting blindness and a greatly impaired usefulness.

**CASES OF OXYCEPHALY.** Sadonia, black, aged nine years. Born in United States. Admitted to Johns Hopkins Hospital September 14, 1911; service of Dr. Harvey Cushing.

*Family History.* Negative. Father died from "heart trouble" aged thirty-two years. Mother, aged twenty-nine years, living and well. No other children. Both paternal and maternal great-aunts died of tuberculosis, but none in parents' families. No cancer or rheumatism. No definite history of rickets. One uncle had convulsions at twenty-seven years, and lost consciousness, etc. No mental trouble in history.

*Personal History.* First child; nine months' baby; normal delivery; no instruments required. Weight, six and a half pounds. Child apparently normal at birth, except for rather large eyes. Head normal. No childhood diseases at all, other than present trouble. Six weeks after birth patient had six convulsive seizures lasting one-half hour each over a period of one month; these convulsions were thought to be due to the stomach; no fever. No recurrence until the present illness. Mild general headaches when child was five and six years of age; no vomiting; no change in shape of head observed. A bright child mentally. Eyesight said to be "hazy at times." No protrusion of eye-balls observed.

*PRESENT ILLNESS.* Patient was apparently in good health until twelve months ago; after complaining of frontal headaches for several weeks, she began to have severe pain in both eyes associated with epigastric pain—this latter pain apparently relieved by catharsis; at times patient vomited when headache was severe. The soreness and pain in the eye-balls has continued ever since. Some frontal headache. Attacks of dizziness were quite frequent during this period. Vision was blurred at times during the past year. Since this time the eyes have become more and more prominent, and recently there is a divergent strabismus, particularly of the left eye.

At present patient complains of pain and soreness of both eye-balls with considerable frontal headache and a sense of fulness at the top of the head and some vertigo. Mother says she has noticed the top of the head becoming taller. "Cloudy sight;" occasional attacks of nausea and vomiting; obstinate constipation.

*Physical Examination.* Well-nourished colored girl, aged nine years. Height, 6 m., 31 cm.

*Head.* An unusually tall head, the transverse diameter being apparently somewhat compressed in the biparietal region. Forehead is very high and 13.5 cm. above nasion is a gradually sloping protrusion to a point just posterior to the site of the anterior fontanelle on the midline. The prominence is 3 cm. in diameter and 5 cm. in height; it is smooth, with the overlying scalp quite movable. Extending forward from this prominence in the median line almost to nasion and backward along the sagittal suture toward the posterior fontanelle is a definite "crista sagittalis," very much like the keel of a boat. (It had apparently been unobserved by her parent on account of the bushy black hair of the patient.) Both the anterior and posterior sutures were firmly closed, and there was no sign of any of the cranial sutures by palpation. Mild dilatation of the veins of the scalp and eyelids, especially the upper ones.

*Cranial measurements:* Hat circumference (horizontal circumference), 52.5 cm., bimeatal arch, 32 cm., chin to nasion, 19 cm., width of orbit, 3.5 cm.; height of orbit, 4 cm.; intercanthi, 3.7 cm.; bialar, 4 cm.



Face: Fairly symmetrical. Usual adenoid expression with divergent strabismus.

Eyes: Marked exophthalmos, particularly of the left eye; eyelids, however, can be closed with difficulty. Widely set apart. Occasional nystagmoid twitches, especially when looking to the left. Convergence very weak, especially of the left eye.

Nose: Typical negro type, flat and wide at the alae. No deviation of septum; child prefers to breathe through mouth, though no definite nasal obstruction ascertained.

Mouth: Teeth in unusually good condition. Palatal arch very high and sharply arched; symmetrical.



FIG. 1



FIG. 2

Figs. 1 and 2.—These figures show the prominent central protrusion at the anterior fontanelle; also the marked exophthalmos with divergent strabismus. The definite crista galli is not clearly demonstrated.

Ears: Rather low-placed, but of normal shape.

Neck: No enlarged cervical lymph nodes.

Chest: Symmetrical, equal expansion. No evidence of a rosary.

Heart and lungs: Negative.

Abdomen: Negative. No enlargement of liver or spleen. No fulness.

Extremities: Negative. Unusually free from evidences of a rachitic diathesis; no enlarged epiphyses, no curving or thickening of tibia, etc. No enlargement of internal condyle of humerus. No other abnormalities.

Neurological examination. Cranial nerves.

1. Negative. Recognized peppermint, etc.

2. Fundi. Right optic disk pale; margins irregular and clear except along the nasal margin, where there is a slight haziness. Much pigment along the temporal margins. Vessels rather full and slightly tortuous. No unusual swelling. Physiological cup shallow from new tissue formation. Left optic disk practically the same as in the right, except more tortuosity of vessels; only a small portion of the lamina cribosa is visible. Lower vessels enter the disk at its lower periphery instead of at the physiological cup. Very mild degree of secondary optic atrophy.

Vision: Practically normal. Perimeter shows a slightly contracted field of vision. Visual acuity is 14/15 in each eye.

3, 4, 6. Pupils moderately dilated, equal and react to light and accommodation. Consensual reaction good. Marked exophthalmos with divergent strabismus, especially of the left eye. Von Graefe's sign, positive. Ocular movements of left eye impaired, especially lateral movements. Convergence poor. Slight lateral nystagmoid twitches at this examination.

5. Normal. Sensation unimpaired; motor unimpaired; taste unimpaired.

7. Normal.

8. Normal. Weber's test heard equally well.

9, 10, 11, 12. Normal. Cerebrum, normal. No paralyses or anesthasias. Memory good. Cerebellum normal. Reflexes present and equal. No Babinski.

First operation, September 15, 1911. Right subtemporal decompression. Usual incision through the right temporal muscle, and the underlying bone was removed by means of the Doyen perforator and burr; bone rongeuired away to a diameter of two and a half inches. Dura was normal but very tense, and upon incising it the cerebrospinal fluid spurted out. A crucial incision was made, and as the intracranial pressure tended to protrude the temporal lobe, the head was elevated sufficiently so that no injury occurred to the cortex, which appeared to be normal. Drain of rubber tissue inserted under the temporal lobe. Usual closure.

Postoperative notes: Uncomplicated recovery. Decompression site very tense. No headache at all and patient feels much relieved. Exophthalmos practically the same. To relieve the intracranial pressure still more, a left subtemporal decompression was advised.

Second operation, September 20, 1911. Left subtemporal decompression. Similar operation performed through the left subtemporal muscle; no complications. Still some intracranial pressure and the brain immediately expanded into the bony opening. Usual closure with drain.

Postoperative notes: No complications. Both decompression openings tense. The venous dilatation of the scalp and eyelids

has disappeared. Headache disappeared entirely as well as the nausea and vertigo.

Ophthalmoscopic examination revealed the disappearance of all haziness along the nasal margins of the optic disks, and a less tortuosity and fulness of the retinal vessels.

Vision practically the same. The divergent strabismus of the left eye is much less and parallelism is now fair; the exophthalmos, however, is practically the same, due, undoubtedly to the very shallow formation of the orbits. No nystagmus observed.

The protrusion at the anterior fontanelle is the same as before the operation. Since then marked improvement, apparently a normal child, except for the cranial deformity and divergent strabismus.

Letter, September 16, 1914, states: "Only two headaches since operation. In excellent health." Vision good. No nausea or dizziness.

CASE II.—Ling, male, aged four years and two months. Born in Nanking, China. Admitted to St. Luke's Hospital, Shanghai, March 4, 1912. Discharged, April 2, 1912.

*Family History.* Meager history obtained, negative. No history of rheumatism or cancer, but one paternal uncle had died of tuberculosis and one of "swollen feet and unable to breathe." Father had syphilis when seventeen years of age; no miscarriages or abortions apparently, father being married at the time. Nine other children living and well; two dead, one from dysentery and the other one from cholera. The patient was the seventh child. Both the mother and father had normal-sized heads, though their eyes were larger than usual among the Chinese, and four other children also had large eyes.

*Personal History.* Normal delivery by midwife; nine months' child; no instruments. No abnormality noted at birth—just the same as the other children. Usual diseases among Chinese children—malaria, dysentery with worms, chicken-pox. No typhoid or cholera.

*Present Illness.* When one year of age, patient became very irritable upon recovering from an attack of diarrhea, during which a number of worms had been expelled; for two days patient cried practically all of the time and did not sleep. Two weeks later a small lump was noticed on the top of the head (at the site of the anterior fontanelle); after four weeks it gradually increased in size to that of a small plum. During this time, patient held its head in its hands and cried very much, especially at night. This continued for one month, and then child became apparently less fretful and apparently normal, except for the lump upon the top of the head. At two years the large eyes of the child were observed apparently for the first time, and during the past two years they have become very large, protruding over half-way beyond their

equator; extreme divergent strabismus, especially of the left eye which is also turned upward. Hearing also has become defective during the past two years. Occasional attacks of headache, but not so severe as at first. No nausea nor vomiting at any time. Child has become absolutely blind during the past year—even for light.

Until six months ago child apparently as bright and quick as the other children, but during the past few months, child has become very quiet and rather sleepy. Still plays, however, with its sticks, but less actively than before. Apparently no paralyses.

*Physical Examination.* Well-nourished Chinese boy, aged four years. Color good.

Neck: No enlarged lymph nodes.

Chest: Negative; symmetrical; equal expansion. No rosary. Heart and lungs negative.

Abdomen: Rather full, but symmetrical. Liver and spleen negative.

Extremities: Negative. Radial epiphyses not enlarged. Internal condyle of humerus, negative. Tibia, both round; no bowing. One undersized testicle, left.

Head: Tall and rather broad in temporal region, so that head tapers toward the vertex. Forehead high but slopes gradually backward. Veins of scalp and eyelids dilated. At the site of the anterior fontanelle is a bony enlargement, the size of a small lemon, 3.5 cm. wide and 2 cm. high, directly in the midline; its bony covering rather bends slightly under firm pressure; the sagittal suture is elevated slightly, both anteriorly and posteriorly of this protrusion. Posterior fontanelle closed and the other suture lines cannot be palpated.

Face: Non-symmetrical; the left molar arch less prominent than the right; nose, however, is not deflected and is a typical Chinese nose, rather flat and delicate.

Eyes: Extreme proptosis, with divergent strabismus, especially of the left eye. Slight conjunctivitis of both eyes. Both eye-balls can be easily shoved forward by forefinger in the external canthus, practically dislocating each eye; apparently this procedure is not painful. No vision at all in either eye, not even to light apparently.

Ears: Both rather low set, possibly only relatively; well formed.

Mouth: Teeth good. Palate high arch and asymmetrical, deflecting toward right.

Throat: Negative, except for slightly enlarged tonsils. Child, however, is a mouth-breather.

*Neurological Examination.* Cranial nerves.

1. Negative as well as could be ascertained.

2. Typical secondary optic atrophy in both eyes, practically the same. Dull whitish optic disks with irregular margins, physio-

logical cup filled with scar tissue. Veins full and tortuous. No increase of pigment. Vision apparently absolutely *nil*.

3, 4, and 6. Extreme exophthalmos with divergent strabismus, especially of the left eye. Pupils widely dilated and do not react to light directly or consensually. All voluntary movements of eye-balls has practically been lost, except slight movements upward and downward and at times to the right. No nystagmus ascertained.

5. Negative.

7. Negative.

8. Very hard to ascertain, but certainly not so acute on both sides as normally.

9, 10, 11 and 12. Negative.

Cerebrum: Still a bright child but rather dulled apparently.

Cerebellum: Negative.

Reflexes: No exaggeration; all of them obtained, equal.

*Treatment.* For fear that the child would gradually become more and more dulled and possibly an imbecile, and also to relieve the headache, I advised a double decompression in spite of the complete secondary optic atrophy; after much difficulty consent was obtained.

Operation March 8, 1912. Father and two brothers insisted upon being present. Right subtemporal decompression. Usual incision made and bone removed; no complications. The vault was very much thinned and revealed the "digital markings" so frequently observed in skulls subjected to high intracranial pressure. The cerebrospinal fluid was under great tension so that it spurted three inches when the dura was incised. After much cerebrospinal fluid had drained away the brain became less tense and pulsated normally. I inserted a strip of rubber tissue beneath the right temporal sphenoidal lobe as in fracture cases and then made the usual closure; no complications.

Postoperative notes: Uncomplicated recovery. Drain removed upon second day. Child apparently in no discomfort. No improvement in the exophthalmos nor divergent strabismus, but the dilatation of the veins of the scalp and eye-balls almost completely disappeared. Fundi retinal veins less dilated.

Fifth day: No headache. Mother thinks child brighter mentally.

Sixth day: During the night, the father came to the hospital with a carriage, and forcibly removed the child, for fear of a second operation.

No photograph had been obtained due to objection of the parents—they were always with the child and they feared an "evil spirit." No trace of the child has been secured.

CASE III.—Bernard, aged ten years. Diagnosis: Mild type of oxycephaly. Operation, right subtemporal decompression. Admitted to Polyclinic Hospital April 27, 1914.

*Family History.* Father and mother alive and well; father has rather large head, high and long. One brother and one sister alive and well. One brother a twin. No miscarriage. No history of abnormally shaped heads or usual disturbances.

*Personal History.* Fourth child; last twin; very long delivery; no instruments used, however. Apparently normal baby, although the large head was noticed at birth. At two years and three months of age, patient had a convulsion: "Was deaf, dumb, paralyzed, and blind for three weeks; high fever." The convulsions at this time were the first patient had had, lasting one and a half days. Since then patient has had about fifty in all, occurring at irregular intervals, one week to three months. These convulsions have been getting worse and more frequent; last week one, week before one, and one today. No prodromal signs; begins with both hands, then legs and lips; often froths at mouth; sometimes bites tongues; convulsion lasts about one hour. Unconscious during spell; afterward weak for several days. Head is gradually becoming larger at the top in front, and more noticeable; deformity increasing in region of forehead. Anterior fontanelle closed at three years of age. Patient is in school in 2B but teacher says he is only fit for 1A. Not at all bright, apparently unable to learn. Likes to roam streets and fights willingly. Talks, but not very well. Very poor memory. Sleeps normally. Bowels regular. Patient has been very unruly, and is becoming worse. Frequent headaches, at times accompanied by nausea and vomiting. Complaints of gradual haziness and blurring of vision; sees double at times. Restless; irritable.

*Physical Examination.* Rather prominent sternal angle; suggestion of "rosary;" some enlargement of lower radial epiphyses. Patient has characteristic "towering" frontal bone; no marked protrusion of the anterior fontanelle.

Measurements: Circumference (hat band), 55 cm.; bimeatal arc, 38 cm.; nasion-basion arc, 40 cm.; basion-mental diameter, 18 cm.; basion-nasion diameter,  $17\frac{1}{2}$  cm.; biparietal diameter, 14 cm.; bifrontal diameter, 10 cm.; bizygomatic diameter, 10 cm.; bi-external canthus, 9 cm.; bi-internal canthus,  $2\frac{1}{2}$  cm.; palate width, 3 cm.; nasion-mental arc, 10 cm.

Reflexes: Active but not unequal; no Babinski, although no plantar flexion of toes obtained. No paralyses. Pupils equal and react normally. A divergent strabismus observable at times, the right eye more than the left; rather prominent large eyes but no definite ptosis or proptosis. Definite lateral nystagmus—greater toward left. Fundus examination reveals a dilatation of the retinal veins and a distinct blurring of the nasal halves of both optic disks; the physiological cups are shallow, being filled with edematous new tissue formation, an early stage of secondary optic atrophy and the cause for the impairment of vision. A subtemporal opera-

tion was advised to lessen the intracranial pressure and thereby not only preserve the vision, but avoid the headaches, and possibly lessen the convulsions and improve the mentality.

Operation, April 28, 1914. Right subtemporal decompression. Usual incision and removal of bone; no complications. Dura quite tense and upon incising cortex, tended to protrude. Large quantity of cerebrospinal fluid escaped. Cortex itself normal. Dura not thickened except slight congestion due to tension; no adhesions. Usual closure; drains. No complications.

Condition at discharge, May 10, 1914. Uneventful convalescence. No convulsions while in hospital.



FIG. 3.—The protrusion at the anterior fontanelle is broad, so that the entire anterior portion of the vault is enlarged, resembling the extreme type of turnschädel deformity.

April 2, 1915. (One year after operation.) Mother says patient is "better in every way since operation; quiet; more sense." No convulsions at all, but patient has had fifteen momentary lapses of consciousness, not sufficient to cause patient to fall (undoubtedly petit mal attacks). No headache at all. Patient seems more observant and has advanced in school. Site of operation flush with surrounding scalp, but tense.

June 19, 1915. Improvement continues. No convulsions and no momentary loss of consciousness during the past six weeks. No headaches. Vision not impaired.

February 4, 1916. Patient is apparently becoming a normal boy. His school work has markedly improved. No convulsions at all—not even the momentary lapses of consciousness. No complaints. Decompression area, however, is still tense, but it does not protrude.

CASE IV.—Isadore, aged fifteen years. Diagnosis, oxycephaly. Operation, bilateral decompression. Admitted to Polyclinic Hospital March 14, 1915.

*Family History.* Negative. No history of abnormally shaped heads nor visual disturbances. Two brothers and sisters well and strong.

*Personal History.* Third child; full term; difficult labor; instrumental. Nursed normally. Scarlet fever at four months of age; apparently excellent recovery; could walk and talk at two years of age. Child seemed perfectly normal up to two and a half years of age, when it was noticed that the head was peculiarly shaped at the



FIG. 4. A lateral Roentgen-ray on the tenth day after operation; the circular-grayish area represents the decompression opening with the small silver clips attached to the dural vessels. The protrusion at the anterior fontanelle with a definite thinning of the adjacent vault can be observed.

top; child cried a great deal, holding its head in its hands. No trouble was suspected, however, until sight began to fail at four years of age. Sight gradually failed, and at five years it was so poor that he could not be sent to public school. At seven years he was just able to distinguish light and darkness and tell when an object was in front of him. At ten years he attended a school for the blind and learned, very rapidly, reading, writing, spelling, geography, history, typewriting, etc. Patient is very bright and at time of entrance to hospital was in last grade of public school.



Reads rapidly (including works of Shakespeare) by means of raised print, and plays checkers with considerable skill. Has learned some carpentry work and has made several articles of wood. Occasional headaches and shooting pains in the head, otherwise no complaints.

*Physical Examination.* Fairly well developed and nourished. No signs of rickets. Right arm slightly atrophied, particularly over bicipital and deltoid regions; head held slightly bent forward. Typical "adenoid" expression and the throat reveals some adenoid tissue. Rather high, narrow, arched palate. Heart, lungs, and abdomen negative.

Head measurements: Circumference (hat-band), 50 cm.; bi-meatal arc, 36 cm.; nasion-nasion arc, 35 cm.; occipitomeatal diameter, 20 cm.; basion-nasion diameter, 20 cm.; basion-nasion diameter, 18 cm.; biparietal diameter, 14 cm.; bifrontal diameter, 13 cm.; bizygomatic diameter, 13 cm.; bi-external canthus, 9 cm.; bi-internal canthus, 3 cm.; palate width, 4 cm.; Apex of nose-mental arc, 23 cm.; nasion-mental arc, 13 cm.

Eye examination by Dr. Kearney March 15, 1915. Definite ptosis and divergent strabismus, left greater than right; definite proptosis of both eyes, right probably greater than left. Eyes stare. Other external conditions normal except in dilatation of the palpebral vessels. Pupils regular, equal and do not react; slightly enlarged. Media clear. Fundus, picture of secondary optic atrophy; practically complete in both eyes. Optic disks both white; margins on lower and temporal side clearly cut. Upper and nasal margins broken down with scar-tissue formation. Cupping slightly exaggerated. Arteries and veins bear normal relations as to size, kinking noted in smaller branches. Fundus tessellated, lighter streaks showing choroidal circulation beneath. Definite lateral course nystagmus—greater toward right.

*Reflexes.* Abdominal reflexes equal and active. Knee-jerks slightly exaggerated but equal. No ankle-clonus; no definite Babinski, though suggested on both sides. No Oppenheim, Gordon, or Chaddock. Wassermann test of blood negative. Wassermann test of cerebrospinal fluid negative; six cells; no globulin.

Lumbar puncture (March 14, 1915): Pressure of cerebrospinal fluid, 37. Elevate head, 41. Lower head, 36. Cough, 38. Blood-pressure, 110 before, 125 after.

Operation March 15, 1915. Right subtemporal decompression. Usual incision and bone removed; no complications. Bone exceedingly thin in places, being the digital depressions due to high intracranial pressure forcing the convolutions into the bone, somewhat like depressions of Paechionian bodies. Dura very tense; otherwise normal, being thin, transparent, not vascular, no adhesions. Cerebral cortex under high pressure tended to protrude upon incising the dura; not edematous. Along the cortical veins, how-

ever, were some areas of whitish induration. Effort to puncture, ventricles and thereby lessen tension not successful. Usual closure with drains; no complications.

Postoperation, first day: Drain removed. Wound bulging slightly but pulsating. Boy talking brightly. Has no pain.

Third day: Several sutures removed; wound healing nicely. Boy distinguishes light from darkness much more readily; could tell for first time in many months when electric light was lighted before him.

Fifth day: All sutures removed. Boy up and about. Very active.

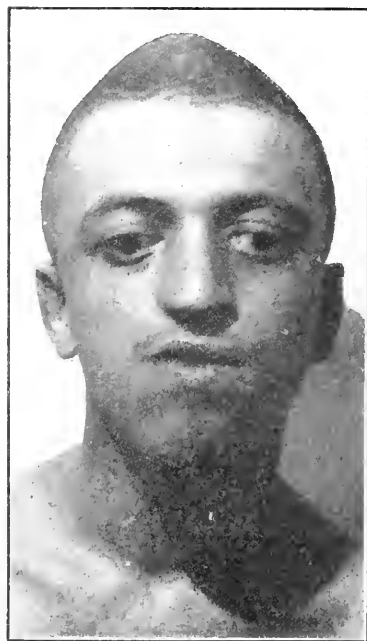


FIG. 5. The marked pointed protrusion at the anterior fontanelle is very striking; the crista galli is also present. The divergent strabismus is greater to the left.

Seventh day: "Reading" his Shakespeare and playing checkers cleverly with other patients.

Ninth day: March 21, 1915. Patient discharged.

April 12, 1915. Second operation. Left subtemporal decompression. Usual incision, bone removed and exceedingly thin in places, showing typical digital depressions which were the most marked of any I have yet seen. The dura was thickened with many adhesions overlying the bone; exceedingly tense, and upon incising it the cortex tended to protrude at the lower part of the dural opening, the cortex causing a slight hernial protrusion. An unusually large decompression opening was made, two and a half to three inches in diameter.

The ventricle was tapped, allowing a small amount of cerebrospinal fluid to escape, thereby lessening the cortical tension, which subsequently pulsated normally. Usual closure with small rubber tissue drain.

Postoperation. Negative.

Discharged April 20, 1915, eight days postoperative.

May 16, 1915. No complaints other than blindness; patient, however, can still tell the presence of light or not. No headaches.

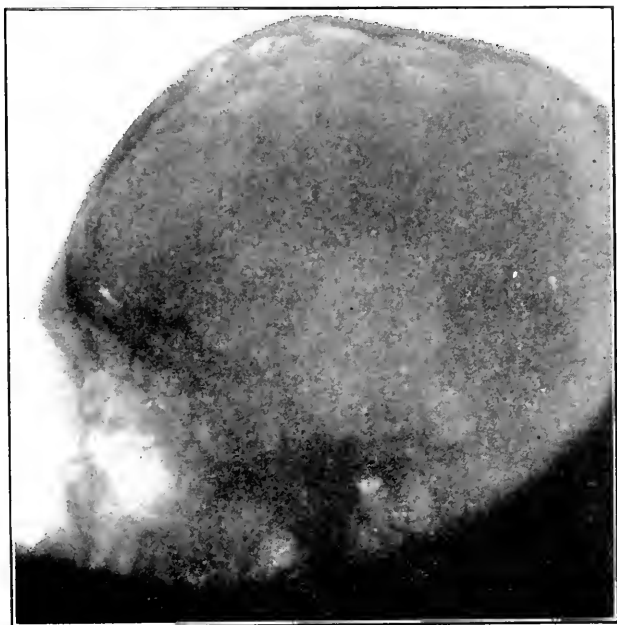


FIG. 6.—A lateral Roentgen-ray on the twelfth day after the bilateral decompression operation; the circular darkened areas are the decompression openings. The protrusion at the anterior fontanelle with the marked thinnings ("digital depressions") of the vault due to the high increase of the intracranial pressure are clearly shown. The lordosis at the base of the skull is evident.

June 19. Condition about the same. Vision unchanged. No headaches.

February 8, 1916. Patient states that he can see better—moving objects, bright colors, etc. This is confirmed. Counts fingers if held very close to eyes. This improvement of vision was not expected, as the condition of secondary optic atrophy was believed to be complete. No headaches; no complaints. Patient is studying Latin, algebra, etc., in the De Witt Clinton High School of New York City.

## TURMSCHÄDEL TYPE OF SKULL; NO OPERATION.

CASE I. —Gottlieb, aged forty-five years, married. German Jew.

*Family History.* Negative. Father (Rector of the University of Prague; professor of mathematics and astronomy) died, aged seventy-two years of senility; mother died aged forty-nine years, of "dropsy;" two brothers living and well; two sisters living and well. Seven brothers and sisters dead—one of consumption, three in infancy, three of unknown causes. Sister has rheumatism. No history of cancer, gout nor of any nervous disease; nor of lues and rickets. Apparently no large head nor large eyes in family history.

*Personal History.* Nine months' child; weight seven and a half pounds. No instruments; head normal apparently. Always well and strong. Very bright and active child; no intellectual impairment. Always stood at the head of his class (University of Prague); A.B. degree and student of medicine; traveled through Europe as tutor. No childhood diseases.

*Habits:* Always a hard-working, strenuous student; a strenuous life. Occasional glass of beer at night; heavy tobacco smoker.

*Neuromuscular negative.* Weight, 192 pounds.

*Present Illness.* When a child, patient had frequent severe frontal headaches, beginning as early as he can remember, and occurring every four or five months; they are, however, of the same character. Patient thought they were due to a blow upon the head, causing the present cranial deformity.

Left facial neuralgia of much severity daily, especially the upper two branches of the nerve; an alcohol injection one year ago brought relief until four weeks ago, when the pain returned, not very severe.

Sharp, shooting pain in both eyes, ever since patient can remember and especially when he was eight or nine years of age; some radiation of pain upward and outward. This pain occurs each day, and at times has a "burning sensation," making eyes water considerably.

Eyes have protruded slightly ever since childhood, and most noticeable at the age of eight years, and especially the left eye, which turned outward. Patient says he is color blind for red. Occasionally sees double when trying to focus with the left eye, false image being to the right. Vision not so good in the left eye, the same for years. Vertigo at times, subjective.

*Physical Examination.* Well-nourished, rather obese white man. Ruddy complexion with the typical Semitic facies. Mucous membrane of good color. Apparently in the best of health. Intelligence excellent.

Chest symmetrical; equal expansion. No rosary. Heart and lungs negative.

Abdomen symmetrical; pendulous. Liver and spleen negative. No free fluid.

Extremities negative. No enlargement of radial epiphyses or internal condyle of humerus.

Head large, turmschädel type of skull very high and broad and tapering upward posteriorly to the vertex. No oxycephalic protrusion at the anterior fontanelle. Forehead retreating, but high. The right side of the skull up to the middle line is more prominent than the left side. No venous dilatation of scalp or eyelids, except at the external canthus of the right eye. Cranial sutures cannot be palpated.

Pupils equal and react rather sluggishly to light. Von Graefe's signs mildly positive. Diplopia upon looking to the left and focussing with the left eye. Slight nystagmoid lateral twitches—equal in both directions.

Fundi mild secondary optic atrophy; retinal veins somewhat dilated; physiological cup shallow; optic disks pale with irregular margins. Frequent nosebleeds as a child, no traumatism. Sense of smell normal.

Ears negative. No discharge or ache.

Patient at present is better than he has been for years. Really no complaint at all, other than the slight facial neuralgia. Naturally no operation advised.

CONCLUSIONS. Cases of cranial deformity of the oxycephalic type are fairly common and are usually brought first to the ophthalmologist on account of the failing vision due to a secondary optic atrophy of varying degree. In my opinion the condition is primarily due to an early meningeal irritation, with the resultant premature closure of the sutures of the base and posterior portion of the skull; as the brain enlarges it tends, therefore, to protrude through the anterior fontanelle and thus the characteristic cranial deformity is produced, and as the result of the increased intracranial pressure a choked disk with the consequent secondary optic atrophy occurs.

The treatment should be directed toward a relief of the increased intracranial pressure; in the cases of the turmschädel type of deformity of the skull there is usually no visual impairment, and the cranial deformity is slight because the intracranial pressure is not high; these cases do not require an operation.

In the oxycephalic type of cranial deformity, however, the increased intracranial pressure should not be allowed to produce the blindness of a secondary optic atrophy; an early relief of this increased pressure with the resulting avoidance not only of the cranial deformity but of the far more important impairment of the vision is advisable by means of the operation of cranial decompression; of the cranial operations to be used, the subtemporal decompression is the operation of choice.<sup>1</sup>

<sup>1</sup> The Operation of Cranial Decompression, AM. JOUR. MED. SCI., April, 1915, No. 4, cxlix, 563.

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## OBSERVATIONS ON THE CUTANEOUS TUBERCULIN REACTION IN THE TUBERCULOUS.

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HYPERSENSITIVENESS to tuberculin when introduced into the body previously infected with the tubercle bacillus has been a recognized fact since Koch's first use of this bacillary extract in 1890. At first only general hypersensitiveness was recognized,

and it remained for von Pirquet, in 1907, to demonstrate local or skin hypersensitiveness. Later it was shown that the mucous surfaces, the eye, etc., also reacted in a hypersensitive way when tuberculin was locally administered, so that now it is assumed that all organs and tissues of a person once infected with the tubercle bacillus will show specific inflammatory or hypersensitive reactions when tuberculin is given locally. The nature of the phenomenon is not thoroughly understood. In a general way, however, it may be said that when the tubercle bacillus gains entrance to the body and incites a local reaction, or, in other words, induces a focus of infection, the body responds in a protective way with the formation of what in a general way may be termed "antibodies" to the poisonous products of the tubercle bacillus. The antibodies are at first circulating, or shortly become so, and are carried to all portions of the body, later to become fixed in the cells of the various tissues, and when tuberculin (antigen) is introduced locally in sufficient quantity an inflammatory reaction occurs. Under certain conditions such as the existence of an acute infection, notably measles or in the last stages of a progressive tuberculous infection, the local hypersensitive reaction fails to occur. Thus in a measure the reaction may be looked upon as an evidence of resisting power on the part of the host.

Unfortunately the greater proportion of all individuals have at one time been infected with the tubercle bacillus, so that the various tests based on this hypersensitive reaction will prove positive in the greater proportion of individuals when tuberculin in sufficient concentration is used. That a focus of infection need have existed before tuberculin will give rise to hypersensitive reactions has been denied by some, notably Much, Sata, etc. However, other observers have claimed to get no hypersensitive reactions unless a lesion has existed. These tests have all been done by the subcutaneous or intravenous injection methods and refer to general hypersensitiveness only. Hamburger, Baldwin, Poten, Roemer, Giemert, Joseph and others come to the latter conclusion. And, too, a few observers have presumably been able to demonstrate a loss of hypersensitiveness after removal of an existing focus, viz., Bahrat, Felix, Klemperer. However, some of these latter tests have been based solely on temperature reactions in guinea-pigs and are not conclusive. The general opinion, however, is that an infection must have taken place before the body in general will react in a hypersensitive manner to tuberculin. And upon this reaction are based the several tests for the existence of a previous infection with the tubercle bacillus. Whether or not the tests have a larger application and will give other information regarding the reaction on the part of the host is yet an undecided question. Lawrason Brown, in a series of 200 cases, could establish no other definite relation.

Ellerman and Erlandsen, in 1909 and 1910, published their observations with a new technic by which they were presumably able to differentiate active, inactive, and latent tuberculosis. The von Pirquet method was used and the strength of tuberculin varied in geometric progression. For instance, four punctures were made, and tuberculin in 1 per cent., 4 per cent., 16 per cent., and 64 per cent. dilutions were applied. Measurements of the papules were made after twenty-four and forty-eight hours, and the average size of the papules and the average differences in papule sizes were calculated. From these figures the hypersensitiveness was determined. This is, according to Morland, really the inverse of the lowest strength of tuberculin causing a reaction. A hypersensitiveness of 100 was said by Ellerman and Erlandsen to be the dividing point between active (100+) and inactive (100-) tuberculosis.

Erlandsen and Petersen and Mirauner published their observations in substantiation of the Ellerman Erlandsen method, and Mirauner would include in the active class all who showed a hypersensitiveness of over 50.

On the other hand, Bessau and Schwenke think that the clinically tuberculous show no hypersensitiveness, but when it does occur it denotes a favorable prognosis. And when hypersensitiveness fails to increase it is of doubtful prognosis. Pringsheim comes to practically the same conclusion.

Hamburger, by repeating tests at intervals, comes to the conclusion that hypersensitiveness increases gradually in early cases, remains low in mild cases, may increase markedly and suddenly when the process becomes active, and disappear slowly when the disease rapidly progresses; and that when hypersensitiveness increases, the prognosis is good and may be an indication for the use of tuberculin.

Among the tests used for determining skin hypersensitiveness is that of Mendel, Mantoux, and Roux, the so-called intradermic test. In this method tuberculin is injected between the layers of the skin, and it has the advantage that a definite quantity of tuberculin can be used with the assurance that it is all absorbed. Thus it affords an excellent method for determining more closely the amount of tuberculin necessary to cause a local reaction. Pringsheim, Jeaneret, Holmes and others worked with the intracutaneous test. Pringsheim used fresh solutions, 1 to 100, 1 to 1000, and 1 to 10,000, and gave the tests eight days apart. In his conclusions he mentions that 10 per cent. of the von Pirquet tests done simultaneously failed to react parallel to the intracutaneous. He also states that 76 per cent. of clinically non-tuberculous children show hypersensitiveness. Holmes showed that activity of the focus increased hypersensitiveness locally. Rosenberg found that 100 per cent. of clinically tuberculous and 62 per cent. of non-tuberculous reacted to a dilution of 1 to 50,000, while 94 per cent.



of clinically tuberculous and 25 per cent. of non-tuberculous reacted to a dilution of 1 to 500,000, and from this he concludes that failure to react to the dilution of 1 to 500,000 would exclude clinical tuberculosis. Kogel says that a strong reaction with a high dilution indicates that healing processes are taking place. Jeaneret comes to the conclusion that the intradermic reaction is in a general way an indication to the grossness of the focus. He also believes that a strong intradermic reaction in a case showing few physical signs is a contra-indication for the use of tuberculin.

Ostenfeld and Permin, in an analysis of 56 cases of skin reactions find that the reactions bear in no definite way on the activity or extent of the disease.

And so conclusions are at variance and the truth not fully understood.

A series of intradermic tests were studied by us at the Adirondack Cottage Sanitarium in an effort to find any existing relation between the quantity of tuberculin necessary to incite a reaction of a certain size and the stage of the disease.

The intradermic reaction was chosen because it allowed more accurate dosage than any other method of skin test. The skin of the forearm was always the seat of the injection, and 1.40 c.c., the volume of solution, remained always the same. Koch's O. T. was the tuberculin invariably used, and care was taken that the injection was always between the upper layers of the skin and that the bevel of the needle could be seen through the skin. The quantity of tuberculin, however, was increased ten times at each successive injection until an erythema of an average diameter of 20 mm. or more was produced. Measurements were taken twenty-four and forty-eight hours after injection.

For convenience the dose is expressed in the form of a fraction as suggested by Dr. Lawrason Brown. The numerator specifies the number of zeros after the decimal point in the metric system, and the denominator the actual amount of tuberculin. Thus 0.0000001 c.c. would be recorded  $\frac{6}{1}$  c.c.

Each patient was at first given an intradermic test with  $\frac{6}{1}$  O. T. or less, and at the end of three or four days, provided a reaction of sufficient degree was not attained, this dose was increased ten times ( $\frac{5}{1}$  c.c.). And if this dose failed to produce the required erythema it was again increased ten times ( $\frac{4}{1}$  c.c.), and so on until an erythema of 20 mm. or more average diameter was produced. It was thought inadvisable to produce a greater erythema than this, inasmuch as the attempt in two instances was coincident with a slight general reaction.

The series was made up of 200 cases, including mostly incipient and moderately advanced cases (3 far advanced). And the reactions were studied in relation to (1) the stage of the disease; (2) the presence or absence of tubercle bacilli, also of rales; (3) the manner

of onset of the illness; (4) the progress of the case in the sanitarium; (5) the probable duration of the disease.

In general it may be said that those cases having both rales and bacilli showed a greater hypersensitiveness to tuberculin than those cases in which neither rales nor bacilli were present, and that the hypersensitiveness was more marked in the moderately advanced cases.

The majority of cases (84 per cent.) reacted to either  $\frac{2}{1}$ ,  $\frac{3}{1}$ , or  $\frac{4}{1}$ , and the majority of these (34.5 per cent. of the total) reacted to  $\frac{3}{1}$ . Using  $\frac{3}{1}$  as the dividing point and watching the direction of the increase in percentages for the different quantitative reactions, we find:

1. That there is a tendency for the moderately advanced case to react to a smaller quantity of tuberculin than the incipient, though the difference in percentage (6 per cent.) is too small to warrant any accurate conclusions.

2. That when tubercle bacilli are present in the sputum the percentage of all cases reacting to less than  $\frac{3}{1}$  is 19 per cent. greater than when tubercle bacilli are absent (47 to 28). And that the difference in reaction is more noted in the incipient cases (48 to 27). Moderately advanced, 47 to 30.

3. That when rales are present on physical examination the percentage of all cases reacting to less than  $\frac{3}{1}$  is 19 per cent. greater than when rales are not present (44 to 25). And that the difference in reaction is about the same for incipient and moderately advanced cases. Incipient, 42.5 to 24; moderately advanced, 40 to 22.

4. That when both rales and bacilli are present the percentage of all cases reacting to less than  $\frac{3}{1}$  is 26 per cent. greater than when neither bacilli nor rales are present; and that the difference in reaction is about the same for incipient and moderately advanced cases. Incipient, 47 to 21; moderately advanced, 45 to 20.

5. That 36 per cent. of all cases react to less than  $\frac{3}{1}$ . That this percentage is increased most markedly when the onset has been hemoptoic (51 per cent.) or catarrhal (40 per cent.). And that the percentage is reduced when the onset has been insidious (26 per cent.), febrile (25 per cent.), and pleuritic (24 per cent.), the last three having almost the same percentage.

6. That the greater percentage reacting to weaker dilutions occurs when the onset is:

Insidious in the incipient cases (incipient 35 per cent. to moderately advanced 22 per cent.).

Catarrhal in the moderately advanced cases (moderately advanced 50 per cent. to incipient 31 per cent.).

Hemoptoic in the moderately advanced cases (moderately advanced 60 per cent. to incipient 40 per cent.).

When the onset is pleuritic the percentage of cases reacting to less than  $\frac{3}{1}$  is about the same in both incipient and moderately

advanced cases. The cases with febrile onset were too few to be considered (4).

7. Considering the reaction from the standpoint of prognosis, that is, the relation of the reaction to the progress of the case while in the sanitarium, we find that:

Of the apparently arrested cases, 22 per cent. reacted to less than  $\frac{3}{1}$ .

Of the quiescent cases, 42 per cent. reacted to less than  $\frac{3}{1}$ .

Of the improved cases, 36 per cent. reacted to less than  $\frac{3}{1}$ .

Of the unimproved cases, 35 per cent. reacted to less than  $\frac{3}{1}$ .

The percentage of incipient and moderately advanced cases reacting to less than  $\frac{3}{1}$  was approximately the same when the cases were apparently arrested or quiescent.

Apparently arrested (incipient 22 per cent.; moderately advanced, 23 per cent.).

Quiescent, (incipient, 45 per cent.; moderately advanced, 40 per cent.).

The incipient improved cases showed 25 per cent. fewer reacting to less than  $\frac{3}{1}$  (21 per cent. to 46 per cent.), and the incipient unimproved cases showed 11 per cent. more reacting to less than  $\frac{3}{1}$  (40 to 29 per cent.) than of the moderately advanced cases.

Considering the apparently arrested and quiescent cases as probably having passed the border-line of activity of their disease at the time of the test, and the improved and unimproved cases as being on the border-line of activity, we may possibly assume that the cases with little involvement, as they improve, lose, and as they get worse, gain, in hypersensitiveness; whereas, the case of longer standing and more advanced disease, on improving, gains, and on not improving, losses in hypersensitiveness. Of course this can only be an assumption.

When the cases are considered purely from the Turban found on physical examination, the percentages reacting to less than  $\frac{3}{1}$  are approximately the same for I, II and III (36 per cent., 34 per cent. and 30 per cent.), but the curve of hypersensitiveness appears to become greater as the Turban increases, for: 34 per cent. Turban I, 23 per cent. Turban II, and 8 per cent. Turban III, react to more than  $\frac{3}{1}$ , the percentages reacting to  $\frac{3}{1}$  increasing as the Turban increases (30 per cent., 38 per cent., 62 per cent.).

When the cases are considered from the standpoint of the duration of the present illness, we find practically no variation in percentages reacting to less than  $\frac{3}{1}$ , when incipient and moderately advanced cases are compared.

CONCLUSIONS. 1. The nature of the focus of infection at the time of the test influences local hypersensitiveness.

2. The quantity of tuberculin necessary to incite a local reaction of 20 mm. diameter bears no definite relation to the stage of the disease. Therefore a single skin test when positive means nothing but the existence of a previous infection.

## NON-TERATOMATOUS BONE FORMATION IN THE HUMAN OVARY.<sup>1</sup>

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IN 1912 two French surgeons, Pozzi and Bender, published a paper in which they discussed at some length the question of bone formation in the ovaries and Fallopian tubes other than that of teratomatous origin, and reported two personal observations of this condition in the ovary. They also stated their belief that such ossification of the ovary is of extremely rare occurrence, since they were able to find in the literature mention of but 5 additional cases which they considered reasonably authenticated, although in a number of other instances specimens had been reported as falling in this category which on investigation were found to have been too imperfectly studied to be accepted. These 7 definite cases are divided by Pozzi and Bender into the following groups: 2 ossified ovarian fibromata, 2 ovarian cysts with ossification of the walls, 2 cases of diffuse ossification in sclerotic ovaries, and 1 ossified corpus luteum.

Since two cases of ovarian ossification happened to come under my observation shortly after the appearance of Pozzi and Bender's article, I was rather surprised by their statement as to the extreme rarity of the condition, and was somewhat skeptical of the accuracy of this view. A fairly careful search through the literature, both antedating and subsequent to their paper, has brought to light a few additional reports, bringing the total of what may be considered fairly well-authenticated cases up to about 14. While this may not represent an absolutely complete list, the number of reports is certainly surprisingly small in view of the considerable amount of literature which exists upon the subject of abnormal ossification in other portions of the body.

The occurrence in ovaries of little hard nodules, often called "ovarian stones," is well recognized as a not exceedingly infrequent phenomenon, but these are usually considered merely calcareous deposits in sclerotic ovaries or degenerated corpora lutea, and are probably in most instances never subjected to microscopic examination, without which the definite determination of the presence of bone is hardly possible. In order, therefore, to ascertain whether or not the occurrence of true bone in the ovary (aside from that formed in dermoids and solid teratomas) is really as unusual as

<sup>1</sup> Presented before the Pathological Society of Philadelphia, May 13, 1915.

has apparently been assumed. I have subjected to microscopic examination, after thorough decalcification, sections from all ovaries containing hard nodules which have come into my hands. In this manner 7 specimens have been studied, with the result that areas of true bone have been found in every one, sometimes of greater extent, sometimes, of lesser, but always clearly demonstrable. The material was derived from the following sources: 5 cases from the gynecological service of the Hospital of the University of Pennsylvania (Dr. John G. Clark), 1 case from the Gynceean Hospital (Dr. Henry D. Beyea), and 1 case from the gynecological service of the Methodist Hospital (Dr. William R. Nicholson). In every instance microscopic examination of sections taken from various areas failed to reveal anything suggestive of a teratomatous process.

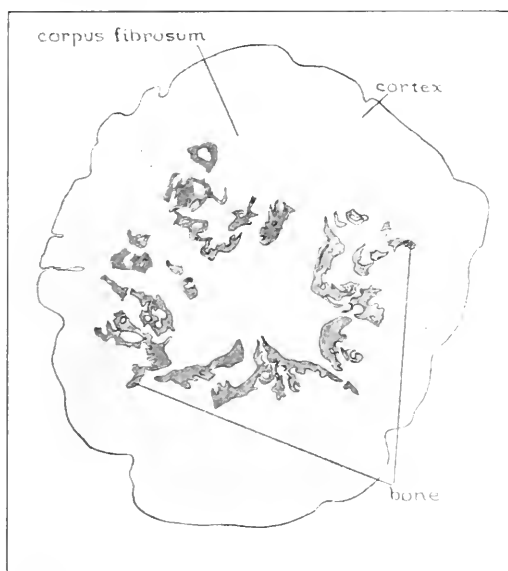


FIG. 1.—Case I. Sketch-drawing of section through the entire nodule. Very low power.

CASE I.—U. Pa., No. 2261. This patient, a girl, aged twenty years, was operated upon by Dr. Clark in 1909, during my term of internship on his service at the University Hospital. The left ovary was somewhat cystic and the right contained a small, very hard nodule. A partial resection of each ovary was performed, with removal of the appendix. The specimen received at the laboratory consisted of "the wall of a corpus luteum hematoma from the left ovary, with a firm, calcified mass, measuring 1.7 x 1.6 x 1.4 cm., from the right;" no histological examination of the hard nodule was originally made, merely a diagnosis of "right

oöphoritis interstitialis chronica (with calcareous degeneration)" being returned by the pathologist. On becoming interested in this investigation I looked up the specimen and found the little nodule intact. Owing to the length of time it had lain in preserving fluids, decalcification was difficult and the soft parts had lost much of their staining properties; the sections obtained, although clearly showing the presence of true bone, were hardly satisfactory for photomicrographic purposes, and therefore merely a sketch drawing of the entire section through the nodule is presented, to show the relations between the ovarian cortex, corpus fibrosum, and the numerous areas of bone forming an incomplete ring or shell within the circumference of the latter (Fig. 1). The tissue in the centre of this bony ring is somewhat looser in structure than that forming the outer portion of the corpus fibrosum, external to the bone. The latter is arranged in wavy, more or less parallel lamellæ, with rather sparse bone bodies; the structure is distinctly compact, but without any very definite Haversian systems.

*Summary.* This case presents an example of ossification within a corpus fibrosum; the ovary was otherwise normal, and there were no marked inflammatory changes in the pelvic organs.

CASE II.—U. Pa., No. 3478. Aged forty-six years. *Clinical diagnosis:* pelvic abscess; pelvic inflammatory disease; tuboövarian abscess. *Operation* (Feb. 7, 1913): vaginal puncture; supravaginal hysterectomy; bilateral salpingoöphorectomy. *Specimen:* myomatous uterus; large right tuboövarian abscess; left hydrosalpinx; *left ovary.* The latter measures 4 x 2.5 x 2 cm.; it is closely adherent to the outer end of the tube, and on section is seen to contain a large degenerating corpus luteum, in which is a considerable area of bony hardness. *Microscopically,* the left ovary shows a fairly normal cortex, closely fused with the wall of the pyosalpinx (Fig. 2). The most prominent feature of the specimen is a good-sized corpus fibrosum, which in some sections shows an almost complete ring or shell of deeply staining calcareous material, with a few small but distinct areas of bone along its inner border. The central area is filled with a loose, richly vascularized tissue, with considerable interstitial hemorrhage. In other sections, cutting through a slightly different plane (Figs. 3 and 4) extensive masses of bone are seen running all through this central softer tissue, which here presents an appearance strongly suggestive of marrow. The bone appears to have formed in the central cavity of the calcareous shell, with which it is everywhere in intimate relationship (Fig. 5). It is fairly compact, with numerous bone bodies in small lacunæ, and indications of Haversian system formation, although this is not very distinct.

*Summary.* This case presents an example of ossification within a fairly extensive calcareous shell formed in a corpus fibrosum; the ovary was otherwise normal, save for dense adhesions to the greatly inflamed tube.

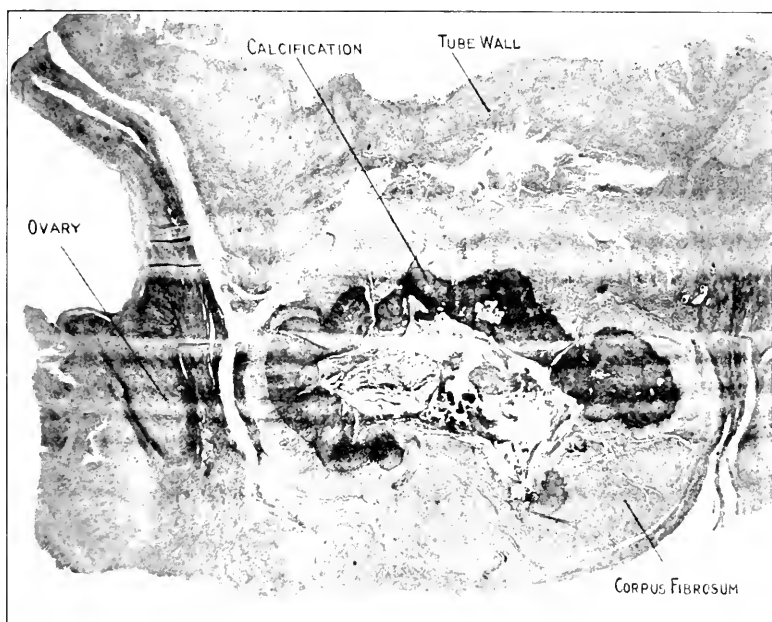


FIG. 2.—Case II. Low-power photograph showing calcareous shell formed within a large corpus fibrosum. (The areas of bone in this section are too small to be distinguishable at this magnification.)

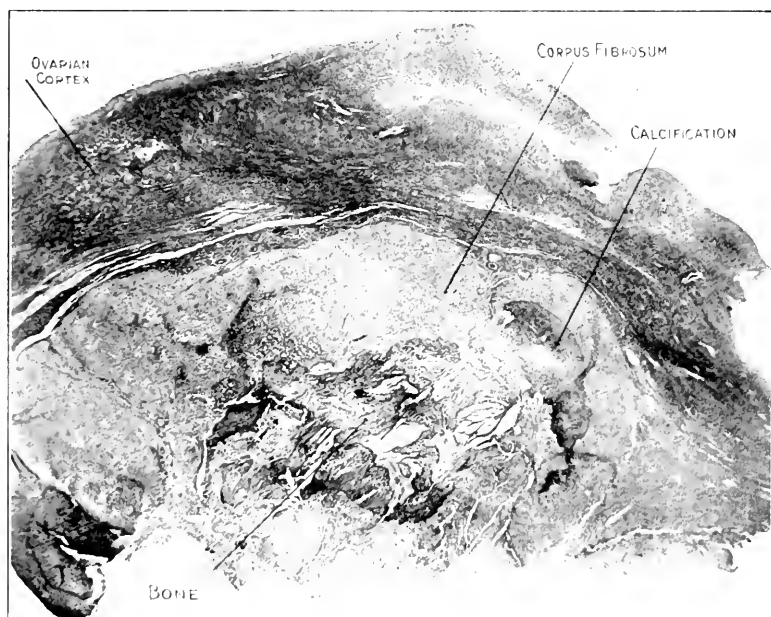


FIG. 3.—Case II. Low-power photograph of a section from a different block of tissue, showing an extensive area of bone in the centre of the corpus fibrosum.

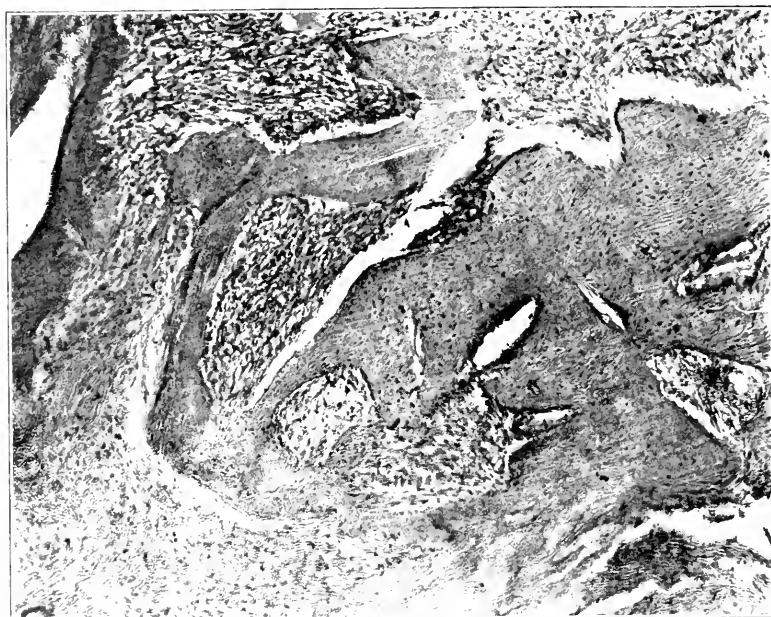


FIG. 4.—Case II. Higher power view of a portion of the bone shown in Fig. 3.

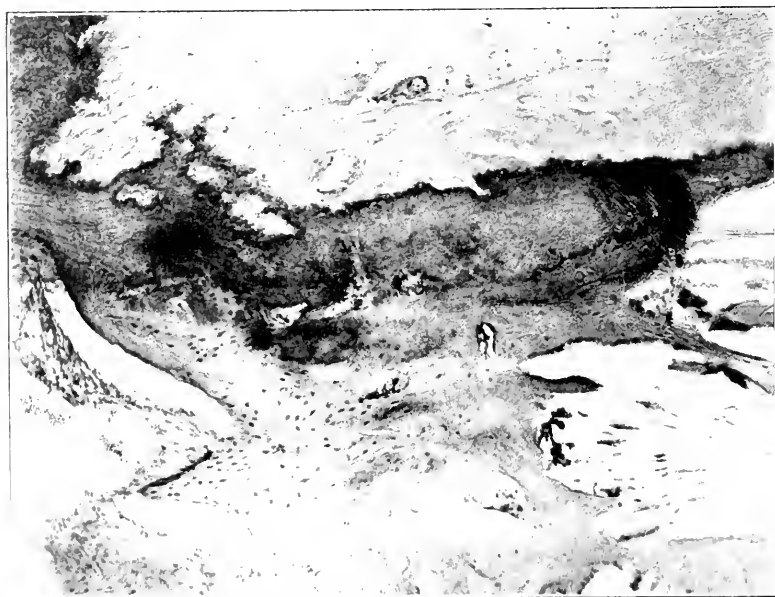


FIG. 5. Case II. High-power view of another field, showing relationship between fibrous tissue (corpus fibrosum) above, zone of calcification in the middle, bone below.



CASE III.—Gyn. Hosp., No. 6577. Aged thirty-eight years. *Clinical diagnosis*: bilateral pyosalpinx. *Operation* (Feb. 25, 1913): bilateral salpingectomy; left oöphorectomy; suspension of right ovary. The left adnexa formed an inflammatory, partially cystic mass, which ruptured during removal, permitting the escape of a considerable quantity of pus; drainage. *Specimen*: both tubes; left ovary; small hard nodule. The right tube forms a typical retort-shaped pyosalpinx 11 cm. in length; the fimbriae are not completely agglutinated, however, and the abdominal extremity is slightly patulous. The left tube forms an indefinite inflammatory mass about 6 x 4 x 3 cm., buried in dense adhesions. The *left ovary* is represented by a mass of torn tissue measuring 5 x 4 x 2.5 cm., which has apparently formed the wall of a cyst or abscess cavity. Accompanying it is a small nubbin of bony hardness, about 2 cm. in diameter, which was shelled out from the left ovary. *Microscopically*, both tubes show intense inflammatory changes. The left ovary (soft portion) shows intense infiltration of the stroma by small round cells. There is one good-sized cyst, apparently of follicular origin. A section through the hard nodule shows the characteristic structure of a corpus fibrosum, with here and there small bits of ovarian stroma about the edge. Throughout the fibrous tissue are extensive areas of calcification, in most of which there is no evidence of bone formation. At one point, however, near the centre of the section, there is a small but distinct mass of true bone, having an irregular outline sharply defining it from the surrounding fibrous tissue, and presenting a similar structure to that of the preceding specimens.

*Summary.* This case presents an example of a small amount of ossification, occurring in conjunction with extensive calcification of a corpus fibrosum in an ovary the seat of acute inflammation, and associated with purulent processes in each tube.

CASE IV.—U. Pa., No. 3880. Aged thirty-four years. *Clinical diagnosis*: multiple fibroid tumors; bilateral hydrosalpinx. *Operation* (March 25, 1914): supravaginal hysterectomy; bilateral salpingoöphorectomy; appendectomy. *Specimen*: myomatous uterus; tubes; ovaries; appendix. Each tube has been transformed into a typical hydrosalpinx, showing microscopically very active and extensive inflammatory changes. The right ovary is buried in adhesions, but is otherwise grossly and histologically normal. The *left ovary* measures 3.5 x 3.5 x 2.5 cm. Its surface is everywhere covered by adhesions; it is slightly cystic, and at one point contains a small bit of hard, bone-like tissue, less than 1 cm. in diameter. *Microscopically*, the left ovary shows a good-sized serous pseudocyst on the surface and a smaller Graafian follicle cyst within its substance. For the rest, the ovary is histologically normal, the cortical tissue being well developed and containing a moderate number of primordial follicles. Scattered throughout

are about the usual number of corpora fibrosa, in the largest of which are seen a few small, irregular plaques of bone (Figs. 6, 7,

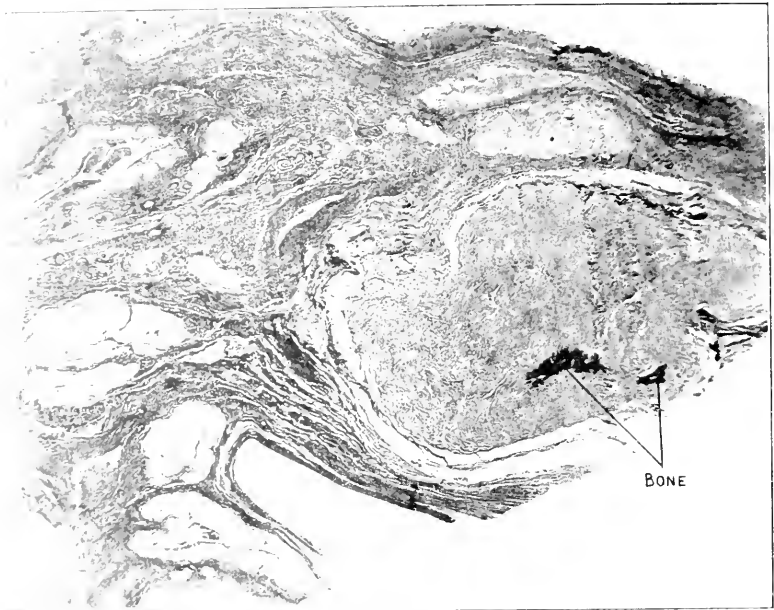


FIG. 6. Case IV. Low-power view of section through entire ovary, showing numerous corpora fibrosa, in the largest of which are two small areas of bone.

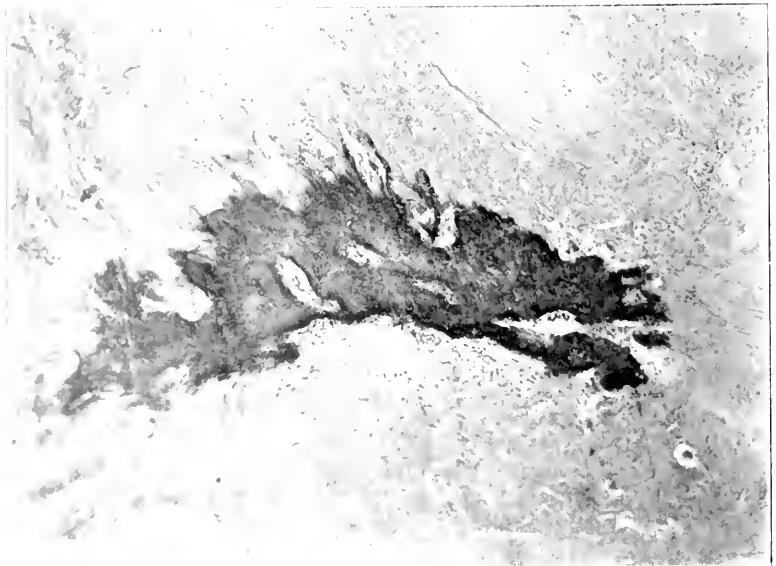


FIG. 7. Case IV. Higher power view of one of the bone areas shown in Fig. 6.

and 8). These lie within the substance of the fibrous tissue or along its edge. They present the same general characteristics as the specimens described above. The bone is arranged in somewhat irregular lamellæ, scattered unevenly throughout which are numerous small lacunæ, each containing a single deeply staining cell. True Haversian system formation can not be definitely distinguished, but here and there are good-sized cavities, each containing a small capillary bloodvessel surrounded by very loose connective-tissue, presenting an appearance very similar to that of ordinary marrow. The bony areas present everywhere an extremely irregular, dentated edge. There are no evidences in this specimen of a previous focus of calcification, such as are present in Cases II and III.



FIG. 8.—Case IV. Photograph from another block of tissue, showing an area of bone on the edge of the corpus fibrosum.

*Summary.* This case presents an example of small foci of ossification, apparently without previous calcification, occurring in a corpus fibrosum in an ovary otherwise normal save for the presence of small retention cysts, but associated with old pelvic inflammatory disease.

CASE V.—U. Pa., No. 3893. Aged sixty-eight years. *Clinical diagnosis:* Carcinoma corporis uteri. *Operation* (April 2, 1911): pan-hysterectomy; bilateral salpingo-oophorectomy. *Specimen:* uterine;

tubes; ovaries. The uterus, including cervix, measures 8 x 6.5 x 4 cm. It contains a small fibroid; the endometrium is greatly thickened, and presents histologically the characteristic picture of advanced adenocarcinoma, with extensive involvement of the muscularis. The tubes show grossly and microscopically moderate inflammatory changes. The right ovary is represented merely by torn remains of a thin-walled cystic sac. The *left ovary* forms a roughly spherical cyst, about 4.5 cm. in diameter, which has been ruptured. The surface is everywhere covered with adhesions. The cyst wall is for the most part thin and delicate, but in one area is considerably thickened, presenting on the inner surface of this portion several whitish, nodular elevations of almost bony hardness. *Microscopically*, sections from both ovaries show a distinctly fibrous ovarian stroma, containing numerous small cystic spaces lined with a single layer of columnar epithelium, and suggesting on first sight a metastatic invasion from the uterine cancer, but on closer examination the lining epithelium is seen to be so regular, and to show so little tendency to active proliferation, that these formations must be considered probably merely cystic ingrowths from the surface epithelium of the ovary. For the rest, the ovarian stroma appears normal, with numerous developing follicles and corpora fibrosa. The cyst cavity has lost its lining epithelium; it presents the typical appearance of a retention cyst of inflammatory origin. Section through the hard masses shows a loose fibrous stroma, with at one point a good-sized developing Graafian follicle. The major portion of the section consists of very numerous irregular trabeculae of bone, presenting an appearance practically identical with that shown in Figs. 4 and 13, and having in the interstices a soft, marrow-like tissue similar to that shown in the latter. The Haversian system formation is rather more distinct in this specimen than in any of the others.

*Summary.* This case presents an example of extensive ossification in a somewhat cystic ovary, associated with pelvic inflammation and an adenocarcinoma of the uterus.

CASE VI. U. Pa., No. 4117. Aged fifty-three years. *Clinical diagnosis:* ovarian cyst. *Operation* (Oct. 31, 1914): Right oöphorectomy. *Specimen:* right cystic ovary, measuring 30 cm. in diameter. The external surface is pinkish white, smooth in places, covered with fibrous adhesions in others. On section the cyst is seen to be unilocular and filled with yellowish, slightly glairy fluid. The cyst wall is for the most part about 2 to 3 mm. in thickness, but at one point there is a hard nodule measuring about 4 x 3 cm. in area by 1.5 cm. in thickness, projecting slightly above the general surface externally, but much more markedly on the internal aspect of the cyst, where it forms a distinct protuberance into the cyst cavity. It presents here the general appearance of being the site of old scar tissue which has undergone considerable contraction, several folds

or plicæ of the cyst wall extending outward from it in a radial manner. It is covered with the same smooth tissue lining the entire

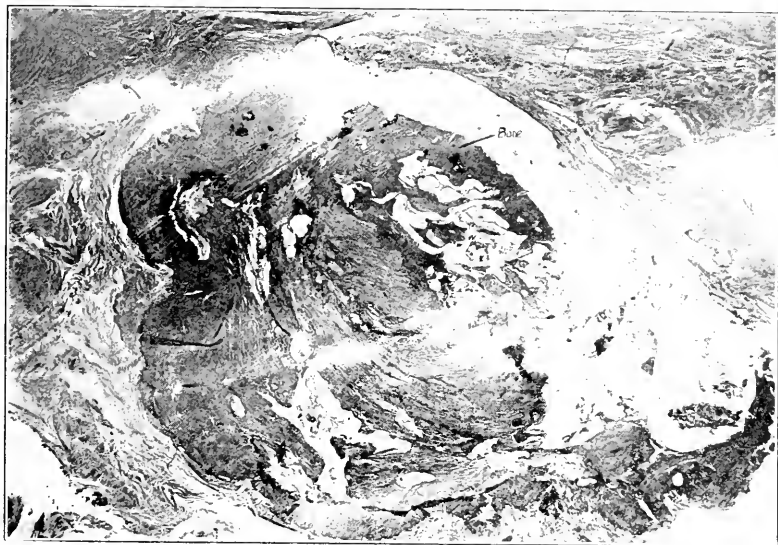


FIG. 9.—Case VI. Low-power photograph of calcified nodule, containing an area of true bone, in the wall of an ovarian cyst.

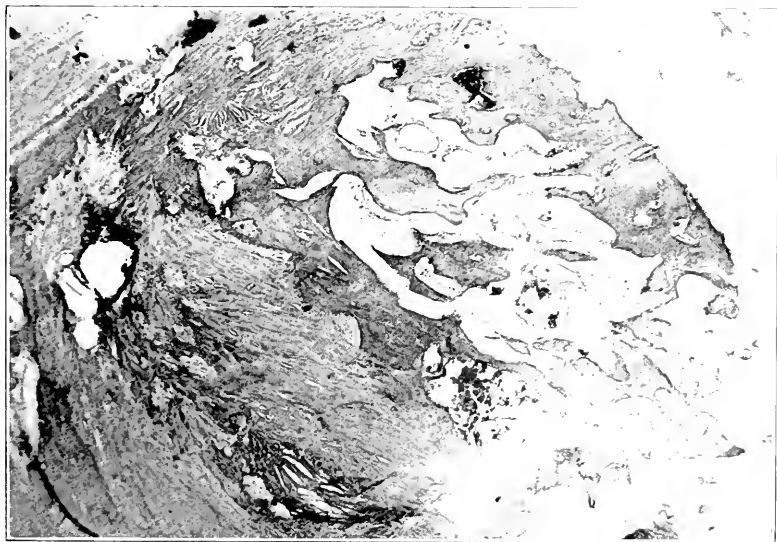


FIG. 10.—Case VI. Higher power view of the area of bone.

cyst cavity, and there is nowhere any evidence of skin, hair, sebaceous matter, or other dermoid constituents. The nodule is

so hard that it can be cut only with a saw. *Microscopically*, sections from the soft portions show the cyst wall to be composed of parallel, wavy bundles of fibrous tissue containing numerous bloodvessels. At one point a somewhat flattened-out cystic follicle is seen. The main cyst cavity is lined by a single layer of low columnar to cuboidal epithelium, such as is characteristic of the serous cystadenoma. Sections through the hard nodule all show extensive areas of calcification throughout the fibrous tissue, which is here distinctly denser and more hyaline in character than in the preceding sections, with here and there good-sized irregular masses of bone (Figs. 9 and 10). The latter has apparently been formed in close relation to the areas of calcification and secondarily to this process. For the most part this bone, which is quite compact, is present in the form of a central plug or lining inside the calcareous shell, exactly as in Case II; but here and there good-sized trabeculae of bone extend out through the surrounding fibrous tissue, with which they are in intimate relation, without any intervening zone of calcification.

*Summary.* This case presents an example of extensive calcification and ossification in one portion of the wall of a cystadenoma serosum of the ovary.

CASE VII.—Methodist Hosp. Aged twenty-two years. *Clinical diagnosis:* retroversion; pelvic inflammatory disease. *Operation* (July 10, 1914): dilatation and curetment; amputation of cervix; appendectomy; suspension of left ovary; removal of hard nodule from Douglas's pouch. This case presents some features of unusual interest. On opening the abdomen the uterus was found to be normal in size and somewhat retroverted; there were a few delicate adhesions in the pelvis, which were broken up without difficulty; the left tube and ovary were normal, but the right adnexa could not be located. The right uterine cornu ended in a little nubbin of tissue, not more than 0.5 cm. in length, apparently corresponding to the stump of the tube, but beyond this no trace of that organ was present, nor were there such dense adhesions in this region that there was any possibility of the tube remaining unrecognized among them. The ovary, likewise, was lacking from its normal situation, and nothing corresponding to it could at first be discovered; but on inserting the hand well down into Douglas's pouch, this was found to be occupied by a tag of omentum, embedded in which was a little stony nodule. It was at first thought that this might be an unusually large phlebolith, although this would be a rather uncommon situation for such a formation; but on more thorough exposure it was seen to be just about the size and shape of a normal or slightly shrunken ovary. It was removed simply by pulling it out from the omental tissue. *Specimen:* an almond-shaped mass, measuring 2.5 x 1.5 x 1 cm., of bony hardness, having a somewhat wrinkled external surface. No soft tissue whatever was

discernible grossly, the nodule presenting the appearance merely of a bit of dense bone or calcareous material. It was sawed in half longitudinally, and on section presented the same solid appearance. Decalcification was tedious, requiring many weeks, but finally it was possible to embed the tissue and cut microscopic sections.

*Microscopically*, a longitudinal section through the entire specimen (Fig. 11) shows the following characteristics: Externally there is a narrow ring of fibrous tissue, arranged in more or less parallel bundles, and containing numerous small bloodvessels and many minute foci of calcification. Here and there bits of fat are adherent to the external surface. For the most part this zone of fibrous



FIG. 11.—Case VII. Very low-power view of a longitudinal section through the entire specimen. The fibrous capsule is seen about the periphery, somewhat mutilated. The grayish areas in the cortex, especially near the right end of the section, correspond to the degenerated tissue mentioned in the description. The bony trabeculae constituting the major portion of the specimen are well shown. The pale area in the centre is loose fibrous tissue.

tissue remains exceedingly narrow, but in one or two places it dips down somewhat into the interior, being here distinctly looser in structure than on the periphery. By far the major portion of the specimen within the fibrous capsule, however, is made up of multitudinous bony trabeculae, the whole greatly resembling a section through a piece of ordinary spongy bone. The trabeculae are fairly thick in the cortical region, forming here good-sized solid masses of bony tissue (Fig. 12); but as the centre is approached they become thinner and more delicate (Fig. 13). The interstices between them are filled with an exceedingly loose areolar tissue, presenting practically the appearance of ordinary marrow, and containing many fat cells, numerous small capillary vessels, and here and there

are of small round-cell infiltration. In addition to these types of areas there are several large areas of granular material, taking on in hematoxylin-eosin preparations a dull bluish stain, and apparently representing greatly degenerated stroma tissue; throughout these a few small foci of calcification are seen. Some of these degenerated areas are completely structureless, while in others the more or less vague outlines of numerous small bloodvessels can be made out, together with many brownish pigmented cells, such as are often seen in the neighborhood of degenerated corpora lutea. In one of the largest of these areas there are a couple of large,

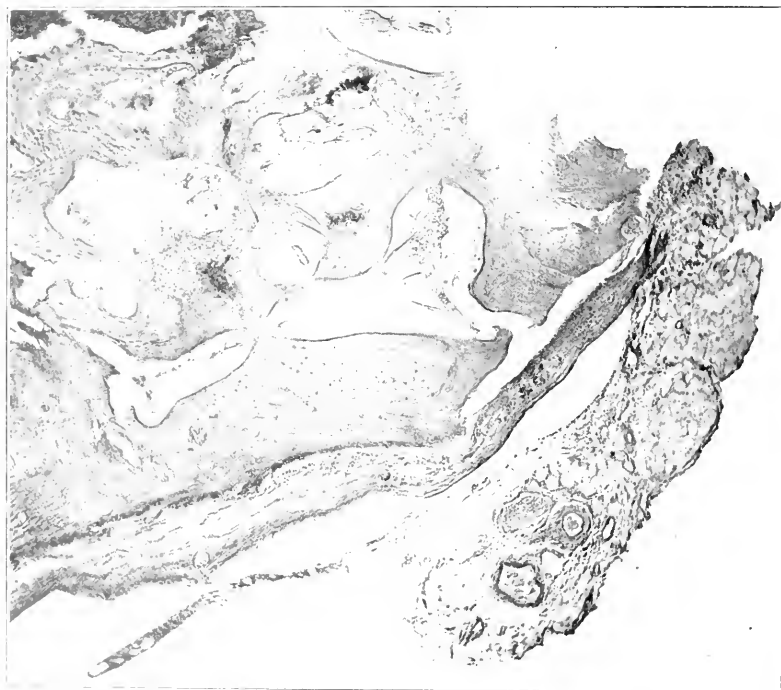


FIG. 12. Case VII. Higher power view of a portion of the cortex, showing fibrous capsule, with bit of adherent fatty tissue, and thick trabeculae of bone.

irregular cavities, with ragged edges and masses of apparently cellular detritus in the centre; the general appearance of these suggests that they may very probably represent the remains of somewhat cystic follicles, but the tissue is so degenerated that it is impossible to determine this with certainty. It is evident that the extensive degeneration of this tissue must have taken place *ante vitam* and not merely as a result of the long sojourn of the specimen in the decalcifying fluid, since the outer zone of fibrous capsule, the fat adherent to it, and the medullary tissue throughout the specimen are all exceedingly well preserved.



*Summary.* This case presents an example of complete atrophy of the right tube, with absence of the right ovary from its normal situation, this structure being apparently represented by an almost completely ossified mass of tissue attached to a tag of omentum deep down in Douglas's pouch.

On account of the almost complete ossification of the little nodule in this case, together with the degeneration of the few areas of soft tissue remaining, it can not, it must be admitted, be identified with absolute certainty as ovary. In view, however, of the entire absence of anything else corresponding to the ovary on



FIG. 13.—Case VII. High-power view of the more delicate bony trabeculae from the central portion of the specimen; showing also medullary tissue between them.

the right side, with the associated atrophy of the tube, and in consideration of the form, size, location, and at least suggestive microscopic findings detailed above, by far the most plausible explanation for this little bony nodule would seem to be that it represents the remains of the right ovary, which has undergone a spontaneous separation from its normal attachments, with secondary degenerative changes. This opinion finds considerable support from a study of the literature, in which reports of a number of more or less similar cases are to be found. The occurrence of partial or complete atrophy of the adnexa of one side, associated with a normal uterus and opposite adnexa, has been noted from

time to time, but until the first fairly comprehensive study of the subject by Rokitansky, in 1860, such cases were always considered due to developmental anomalies. Rokitansky reported 15 cases in which some degree of atrophy had occurred, usually associated with detachment of the adnexa from their normal relations, and showed that definite pathological processes, occurring either during intra- or extra-uterine life, but *subsequent* to the primary formation of the organs in question, may be responsible for this condition.

Since that time quite a few writers have interested themselves in this subject, and our knowledge of it has been enriched by numerous reports of cases. In the chapter on Diseases of the Ovary in Veit's *Handbuch*, 2d ed., Pfannenstiel says that in cases of this sort "both organs (tube and ovary) are usually lacking from their normal situation, or only the ovary may be entirely absent; if present at all, however, the latter is usually at least atrophic, shrunk, or otherwise pathologically altered. It is often found to have formed an anomalous attachment somewhere in the abdomen; for instance, to the omentum, on the pelvic brim, in Douglas's pouch, or on the urinary bladder. Under these circumstances it is usually greatly shrunk, necrotic, and at times calcified, or transformed into a sac filled with old blood clot." Frankl, in his recently published *Pathological Anatomy and Histology of the Female Genital Organs*, declares that "cases of complete amputation of the ovary, which then lies as a shrunk mass in Douglas's pouch, are not exceedingly rare," and in a paper published last year, Ogórek was able to collect nearly a hundred examples of spontaneous amputation of the uterine adnexa from their normal attachments. After careful consideration of all features of the question, Ogórek, in common with most modern authorities, has come to the conclusion that such separation may occur in only two ways: either as the result of (1) *torsion*, or (2) *strangulation by inflammatory peritoneal bands*, the former occurring when free mobility of the adnexa exists, the latter when these organs are more or less fixed by adhesions to surrounding structures. Once such separation has taken place, he says, the bit of tube left attached to the uterus shrinks to a small nubbin, whose appearance is identical with that of the stump often left after a salpingectomy. The detached distal portion of the tube in many instances undergoes necrotic changes and is absorbed; in others it may remain as an unrecognizable tissue mass somewhere in the pelvis, or may even wander into some distant portion of the abdomen.

The first of these conditions—*i. e.*, a small nubbin of tube at the uterine cornu, with complete absence of the remainder—is exactly that which was present in the case under discussion. In place of the ovary at its normal situation, the oval mass of bony tissue described above was found attached to the omentum deep down in

Douglas's pouch. It is easy to comprehend that following a spontaneous amputation of the right adnexa, whether due to torsion or strangulation, but probably the latter, the ovary in this instance, instead of undergoing necrosis and complete disappearance like the tube, formed new attachments to the omental tissue. With the great disturbances in its nutrition that must have followed, however, degeneration, calcification, and finally ossification were not unnatural sequelæ, and no doubt represent the actual sequence of events. While I have not been able to find any record of an exactly parallel case of histologically demonstrated *ossification* of a spontaneously amputated ovary, it seems most probable that such would have been brought to light had more careful studies of such organs been made. Rokitansky, indeed, in his paper of 1860, speaks of several cases in which the detached or twisted ovary showed a calcareous or bony consistency; but it is evident from his descriptions that at least some of these were dermoids, and, at any rate, pathological knowledge was too undeveloped at that time to make his opinion on this point of value. In the more recent literature at least two cases have been reported which present striking points of similarity to the one under discussion: both these are described by their authors as cases of *calcification* of the ovary, but as no microscopic examination was made in either instance, the possibility that in reality ossification may have been present can not be excluded. These cases are briefly as follows:

Prince (1895). "Miss B., aged forty years; examination revealed a uterus studded with small fibroids. . . . On passing my fingers (at operation) over the posterior surface of the uterus they came in contact with a hard body, loosely adherent, and easily separated from its attachments to the uterus. The right ovary was present and cystic. This with the tube was removed. The left ovary and tube were absent; all that remained was a short stump of the tube about one-fourth inch long. On examining the hard body removed from the posterior surface of the uterus it was found to be the exact size and shape of the ovary. It was free in the pelvic cavity save for the very slight attachment to the uterus by its rough surface. The ovary must have attained full size in its normal position, when for some cause it became detached with the tube, probably from some constricting agency, which has done a neater amputation than could have been done by any surgeon. All vestige of any constricting band, or of the amputated tube, had disappeared."

Miländer (1903). The patient was aged twenty-one years; a nullipara. A large cyst with twisted pedicle was present on the right side; "the left broad ligament was very delicate, the left tube very thin, and its distal extremity not to be found. On careful examination a flat, almond-shaped body was found on the left side in Douglas's pouch, with its long axis transverse, lying free on

the peritoneum, from which it was removed with forceps. This free body was found to be the calcified left ovary; in places it was of stony hardness, in others less dense. It measured 2.8 x 1.6 x 0.8 cm.; the surface was rough and irregular. On section various small, hard masses could be lifted out with forceps, evidently calcified corpora lutea." The author suggests that the calcification was due to disturbances in nutrition caused by pressure of the cyst on the opposite side.

Returning to the question of ossification of normally situated ovaries, there are, as has been said, surprisingly few cases on record. Those mentioned by Pozzi and Bender, in addition to their own, were reported by Fürst, Pfannenstiel, Schroeder, Strauch, and Waldeyer. In going through the literature, I have come across the following additional instances, the essential features of which are here given as briefly as possible:

Winckel (1886). A completely ossified ovary, the size of an adult head, measuring 40 x 40 x 15 cm.; the interior cystic, the cyst wall of bony hardness, showing in thin sections (ground, not decalcified) typical lamellæ and bone bodies.

Coe (1892). One ovary the seat of cystic degeneration, the other of chronic ovaritis; the latter contained a small, hard nodule, which microscopic examination showed to be true bone. Centre of nodule gelatinous, consisting of bone marrow. No evidences of dermoid.

Copeland (1892). Hard growth in each ovary, so dense that it was almost impossible to cut through them with a jeweler's saw. A thin piece secured by grinding presented the histological appearance of longitudinally cut bone.

While the presence of true bone in these cases of Coe and Copeland appears to have been fairly well confirmed by microscopic examination, Williams (1893) contended that both were merely examples of calcification, and expressed his belief that "it is very doubtful if true ossification occurs, although a few apparent cases have been reported."

Robertson (1912). Right ovary 12.5 x 15 cm., of bony hardness. When sawed through, found to consist of a solid wall with a cavity in the centre filled with grayish material. A section of the bony mass made by grinding a thin fragment on a water stone showed atypical bony tissue with irregular spaces and canals; no typical Haversian systems; no evidences of teratoma. The author thinks the bone represents a metaplasia of fibrous tissue.

Moschowitz (1913; 2 cases). Case I.—Double salpingo-oöphorectomy for tubal tuberculosis. In the right ovary a dense nodule having a convoluted surface. On section "the outer third of this nodule was found to be composed of lime salts with many cavities, around which conversion into true bone is taking place. The central portion of the mass consists of true bone, with lamellæ,

bone cells, and Haversian canals containing well-formed blood-vessels, fibrous tissue, and fat. The ossification is evidently spreading eccentrically." Case II.—Hard mass the size of a pecan in centre of ovary. Findings similar to those in Case I, but more advanced.

Adachi (1913). Left ovary measures 2 x 1.5 x 1 cm. At one edge a somewhat hard mass palpable; after decalcification easily recognized as a corpus albicans, with an area of calcification and irregular trabeculae of well-formed, compact bone, containing spaces evidently marrow cavities, and Haversian canals. In the marrow tissue connective-tissue cells, myeloblasts, myelocytes, plasma cells, lymphocytes, erythrocytes, etc.; no osteoblasts. Bony tissue is in central portion of the area of calcification.

In addition to the above-mentioned cases it is of course possible that other instances may be scattered through the literature, but in view of the fact that I have been able to collect from a moderate amount of pathological material no less than 7 additional ones in a comparatively short space of time (all but one of these occurring within two years), it certainly seems that the condition must be far more common than might be assumed from a study of the literature.

The question naturally arises as to the origin of the bone in cases of this type. The first thought might be that it is always a teratomatous manifestation, in view of the frequent occurrence of such tumors in the female sexual glands and of their well-known tendency to produce bony tissue. Even in cases such as those reported in the present communication, where careful microscopic examination has failed to reveal the least indication of other abnormal tissues, the argument might be advanced that we are here dealing with examples of the so-called "reduced" teratoma, in which it may be assumed that all varieties of tissue save one have been suppressed, as is believed to be the case in certain thyroid-like and other anomalous growths of the ovary. This theory I have discussed at some length in a previous paper, and do not therefore wish to enlarge upon it here. Suffice it to say that while this hypothesis has many points in its favor in the case of growths consisting of highly organized glandular tissue, such as thyroid, a much simpler and more plausible explanation for the occurrence of bone in the ovary would appear to be that it arises as a result of metaplastic changes in the fibrous tissue with which that organ is so well supplied. The tendency of old fibrous tissue, especially if the seat of chronic inflammatory processes, to undergo calcification is of course well known. The occurrence of true ossification in such areas is also a matter of frequent observation, and, indeed, abnormal ossification has been noted in almost all parts of the body, especially the muscular system, bloodvessels, old scars, etc., and cases have been reported involving the kidney, penis, thyroid,

pleura, lymph glands, and various other organs.<sup>2</sup> In several of the cases considered in the present paper the ossification was located in the substance of a corpus fibrosum, *i. e.*, in an area of more or less inert, avascular fibrous tissue; in others, in the fibrous tissue of a cyst wall, or in an atrophic, degenerated organ. In a number of cases the ovary affected was associated with a chronic pelvic inflammatory process of high grade. In almost all instances the ossification was evidently secondary to more or less extensive calcareous deposits in the fibrous tissue, and in the instance where this was most markedly absent (Case IV) the ovary was otherwise wholly normal, save for perioöphoritic adhesions, and in no way suggested the existence of a teratomatous neoplasm.

In addition to the above arguments it may be mentioned that most authors who have interested themselves in this subject have likewise arrived at the conclusion that the bone is purely metaplastic in origin rather than neoplastic. The best term to apply to the condition would therefore appear to be "ossificatio ovarii" rather than "osteoma," notwithstanding the use of the latter by Pfannenstiel and one or two others.

CONCLUSIONS. As a result of the study of 14 cases from the literature and of 7 personal observations it appears that true ossification of the ovary may occur independently of any neoplastic or teratomatous process. Such bone formation is probably metaplastic in character; it occurs chiefly in corpora fibrosa or fibrous portions of the stroma, and particularly in ovaries from cases of pelvic inflammation. In one instance of the personal series it involved the wall of a serous cystadenoma, and in one a spontaneously amputated ovary which was found adherent to the omentum at the bottom of Douglas' pouch, associated with complete atrophy of the corresponding tube. It is highly probable that true ossification of the human ovary, of non-teratomatous origin, is far more common than has generally been believed.

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## GANGRENE OF THE LUNG FOLLOWING ARTIFICIAL PNEUMOTHORAX.

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GANGRENE of the lung in pulmonary tuberculosis is a very rare condition. Gangrene of the compressed lung in a patient treated with artificial pneumothorax is exceedingly rare; in fact, no case, to the writer's knowledge, has thus far been reported in literature. The following is a report of such a case, with autopsy.

The patient was an American, aged forty-one years; single; teacher. His father died of pulmonary tuberculosis, aged sixty-nine years.

The patient had had numerous attacks of gonorrhea many years before.

The present illness began with a cold. This he was unable to throw off, and three months later definite physical signs were found, and there were tubercle bacilli in the sputum. On his way north to Saranac Lake he went to the Johns Hopkins Hospital, where the Wassermann and gonorrhea-fixation tests were found negative. On his arrival at Saranac Lake he was not below normal weight, had considerable cough and expectoration, and an afternoon fever of 100° to 101°. The chest examination showed a hyperresonant note over the left side, fair breathing, and coarse rales over the

entire front. On the right side posteriorly indefinite rales were heard to the seventh vertebral spine. There was a slight scoliosis, with convexity to the right. The rest of the physical examination was negative.

The urine was normal. The sputum contained many tubercle bacilli, and numerous secondary organisms, chiefly streptococcus and staphylococcus.

No special comment is needed here. The case was an ordinary one of advanced active tuberculosis, involving the greater part of the left lung, and a probable involvement of the upper part of the right. The patient was put to bed and a cough sedative given.

During the next two months he did poorly. The cough became very troublesome and the expectoration increased greatly in amount. The temperature ranged daily between  $101^{\circ}$  and  $102^{\circ}$ , with morning remissions. The left chest showed dullness and medium coarse rales over most of the side, with signs of cavitation from the clavicle to the fourth rib. The right chest showed fine rales and deep rhonchi to the seventh rib.

The left lung was disintegrating, and the patient was failing rapidly. With the hope of controlling the advancing process in the left lung, artificial pneumothorax was performed. The history of the seven punctures made is as follows:

Entrance was made in the seventh interspace in the anterior axillary line. The pleural cavity was easily found on the first try. The water manometer read  $-3$  to  $-11$ ; 350 c.c. of warmed nitrogen gas were injected. Pressure was left at  $-2$  to  $-6$ . Two days later 500 c.c. were injected, the pressure being  $-36$  to  $-9$  before and  $+2$  to  $-1$  after the injection. Four days later on entrance the manometer read  $-3$  to  $-8$ . About 500 c.c. had flowed in when the patient suddenly gave a sharp cry and seized his side near the needle entrance. He held his breath for a moment and groaned as if in great pain. The pain quickly passed off. The pressure was  $+2$  to  $-2$ . This was watched for a few moments, but there were no changes. Apparently there were no ill-effects from this refill.

A week later on entrance the manometer read  $+3$  to  $-3$ . This increased pressure was doubtless caused by the presence of a small amount of fluid. At the next operation, the pressure being  $-3$  to  $-10$ , 400 c.c. of gas were given and the pressure left at  $+2$  to  $-2$ .

Meanwhile there had been no noticeable abatement in the symptoms. Although the patient said he felt much better his cough was very hard and explosive, the expectoration was increased, and the temperature persisted. Breath sounds being heard over the upper part of the left chest it was decided to put a greater pressure upon the lung. Accordingly 800 c.c. were given, the pressure being  $-5$  to  $-10$  before and  $+6$  to  $+2$  after the operation. The patient had no distress although feeling "tight," a sensation that lasted but a few hours.



Two weeks later the fluid was as high as the seventh rib. To satisfy the patient, 200 c.c. of gas were injected and pressure left at +5 to 0. At entrance the manometer showed +1 to -4.

This is the record of the nitrogen injections. It is to be noted that except for the sudden pain during the third operation (considered as a torn adhesion) there was nothing untoward in signs or symptoms caused by the treatment. A small amount of fluid formed, but this is encountered in the majority of cases. The pressures were moderate. The amounts of gas taken were small, but from the signs and symptoms it was judged that the collapse was not complete, and fluid was present which at no time was great enough to be withdrawn.

The patient was too ill to have Roentgen-ray pictures taken. The chest examination, besides the fluid, showed diminished and absent breath sounds over most of the left chest except at the apex and along the vertebral groove. The signs in the right chest remained the same.

His symptoms continued without abatement and his general condition became progressively worse. One afternoon, nine days after the last injection of gas, he suddenly raised a large amount of exceedingly foul, greenish sputa. The next morning, during a coughing spell, he filled five or six sputum boxes with the same putrid matter. He said that it burnt his mouth like fire. The stench was noticeable throughout the house. For nearly three weeks this state of affairs continued. He used about two boxes a day. At times the intensity of the odor diminished. On three occasions he raised from a half to one ounce of blood. Toward the end the expectoration became chocolate colored and watery.

The sputa examined showed mostly pus, enormous numbers of acid-fast bacilli, and also *Oidium albicans*, *Staphylococcus pyogenes aureus*, and a Gram-negative bacillus which produced gas smelling like methane.

No breath sounds were heard on the left side. A metallic tinkle was present. A moderate amount of fluid was made out. There were a few scattered rales on the right side.

The patient sank lower and lower, and finally died three weeks after the first evidence of gangrene of the lung.

**AUTOPSY.** Aside from a few scattered fresh tubercles on the surface of the liver and slightly enlarged and partly caseous mesenteric glands, there was nothing abnormal found on the examination of the body except the thorax, where the findings were as follows:

On opening the thorax the heart is found pushed over almost to the midline. The left lung is collapsed and lies against the vertebral column and mediastinum. The pleural cavity contains about one liter of brown, foul-smelling fluid. The collapsed lung occupies about one-third of the left thoracic cavity, being 20 x 9 cm. The division line between the lobes is obliterated. The lung is gray

green in color and "mushy." There are adhesions running upward and outward from the apex to the parietes. One adhesion is as large as a finger, and of solid fibrous tissue. The other is small and strand-like. The apex of the lung is very adherent. The base of the lung is bound down to the diaphragm by tremendous adhesions. The lung shows five large cavities opening directly into the pleural cavity. They range in size from 1 x 2 cm. to 7 x 4 cm. Four of these openings occupy the anterior surface of the lung while the fifth and largest is located at the posterior fissure between the lung and parietal pleura. The edges of these holes are bevelled and shreds of gangrenous lung tissue are protruding from them. On the parietal pleura, corresponding to the edge of the hole at that place, is a cicatrized ridge as if lung tissue had been torn from visceral pleura which had become adherent to the parietal pleura.

The parietal pleura is 2 to 3 mm. thick. The pleura covering the lung is very dense. Both pleurae are grayish green in color and covered with slimy exudate.

In removing this lung the parietal pleura was removed also. The lung tissue seen through the various openings is everywhere the same, being composed of grayish green, sponge-like tissue, all evidences of normal lung tissue being destroyed. A section through the apex shows no cavity, but the tissue is more or less solid and mottled and areas of caseation are present.

The right or uncollapsed lung is voluminous. The color is bluish pink. There is a fine adhesion at the apex. Over the posterior portion of the lower lobe the pleura is roughened and lusterless. There is no fluid in the pleural cavity. The middle lobe in its central and lower portions shows dense tuberculous areas. On section, scattered tubercles are seen throughout the upper and lower lobes, averaging 1 to 2 cm. in diameter.

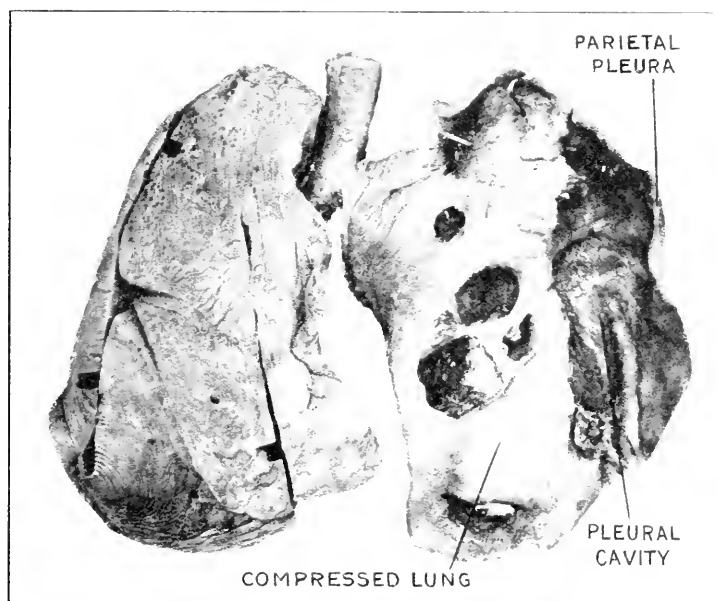
The tracheobronchial glands are grayish black in appearance and moderately enlarged, but do not in any way block or narrow the bronchi by pressure. There is no occlusion of the bronchi or blood-vessels entering the lungs.

**MICROSCOPIC EXAMINATION.** A section taken from the apex of the gangrenous lung shows first a greatly thickened pleura composed of dense connective tissue. Scattered throughout the pleura are numerous minute tubercles. Beneath the pleura no normal lung structure is to be seen. There are small slit-like spaces which are compressed alveoli. Distributed throughout are areas of granulation tissue containing small capillaries in which red blood cells are found. In this granulation tissue are also seen fresh tubercles. Dipping down from the pleura is a dense fibrous band. There are also to be seen large tubercles composed of a central area of fibrous tissue and a dense outer ring of round cells. At the edges of the central area are seen giant cells. The bloodvessels show obliterative endarteritis. Throughout this whole layer there is a dense round-cell

infiltration. This layer quickly shades off into an area of non-staining homogeneous tissue in which are scattered portions of nuclei.

DISCUSSION. Was artificial pneumothorax the cause of the gangrene in this case? A brief review of the subject of lung gangrene may help to decide this question.

Gangrene of the lung implies not only death of the tissue but subsequent putrefaction. The necrosis is due to the obstruction of bloodvessels and the deprivation of blood supply. This obstruction may be inflammatory or mechanical. The gangrene is due to the invasion of the necrotic area by putrefactive organisms. Among the



Photograph of lungs showing gangrenous compressed left lung with holes opening into pleural cavity through which may be seen the gangrenous tissue.

organisms found are the pyogenic staphylococcus and streptococcus, the coli communis, and a pseudotubercle bacillus.

A frequent direct cause of gangrene is the retention of putrid secretions within a bronchiectatic cavity; also the inhalation of septic material, either during anesthesia or on account of paralysis of the glottis.

Inflammation of the lungs such as pneumonia may lead to gangrene, although some observers doubt its occurrence. It is interesting to note the rarity of gangrene in pulmonary tuberculosis. One would think that bronchial dilatation, caseous areas, and cavities would offer a good field for its occurrence, yet this complica-

tion is extremely infrequent. But autopsies show that a localized area of gangrene may exist in a lung without producing fetid sputum or breath, as seen in Fox's series, in which 6 cases of gangrene were found out of 100 postmortems in tuberculous subjects. This is a much higher percentage than other authorities have found. Four of the cases had gangrene in pneumonic areas and two on the walls of cavities.

Tumors of the mediastinum may by pressure lead to gangrenous changes; and septic emboli plugging a pulmonary vessel may cause gangrene. In our case the bronchi and root vessels were patent, and no focus was found at autopsy from which septic emboli could arise.

Occasional cases have been reported in which putrid pleural effusions have been withdrawn, and a fistula being established portions of gangrenous lung have been discharged through the opening. These cases coming to autopsy show the lower portion of the lung compressed by the fluid; the fluid is putrid; and the contiguous lung tissue gangrenous. Loculated fetid empyemas tend to burrow through the lung to a bronchus, and on account of the dense adhesions pneumothorax rarely results. Whether these putrid effusions are primary or secondary is often difficult to say. In the case here reported fluid was noticed after the third refill, but there was nothing in signs or symptoms to lead us to believe that it was gangrenous in character.

Bearing more directly is the question whether gangrene follows collapse or compression of the lung by air as in pneumothorax, or by fluid as in pleurisy with effusion. A review of the literature of many years fails to reveal a single case of gangrene of the lung after a natural or artificial pneumothorax. Evidently the entrance of air into the pleural cavity cannot of itself cause gangrene of the lung.

Fox gives pleurisy with effusion as one of the causes of lung gangrene, but cites no cases and doubts if pressure of fluid in the absence of other factors can produce gangrene. I am not aware of any reports illustrating this condition. The nearest approach to it is found in the cases of putrid effusions or empyemas mentioned above.

Whatever the cause of the obstruction the decomposition of retained secretions is believed by Fowler and Godlee to be the main factor in the production of gangrene of the lung.

In the case here reported there were three factors present which, in combination, were probably sufficient to cause the gangrene. They were (a) necrotic areas due to obliterative endarteritis; (b) pressure of gas and recoil of lung which aided necrosis, and (c) putrefactive organisms.

The following sequence of events might have occurred:

1. To begin with there was a rapidly disintegrating lung with superficial cavities.

2. More or less extensive necrosis of lung tissue due to obliterative endarteritis.

3. The introduction of gas collapsed the lung, limiting the blood supply, and thus aiding in the extension of the necrosis.

4. Putrefaction now took place and gangrene supervened upon the necrotic areas.

5. Rupture of the lung then followed and the pleural fluid became putrid and corroding.

Putrefactive organisms and large necrotic areas are frequently present in tuberculous lungs and do not produce gangrene. There is no reason to suppose that had this lung been let alone it would have become gangrenous. It would appear that the collapsing of the lung was the immediate exciter of the subsequent events.

Other lungs in a similar condition have been collapsed without bad results, but evidently such a procedure is fraught with danger.

I am indebted to Dr. Lawrason Brown for the privilege of reporting this case.

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## REVIEWS

LEHRBUCH DER SPEZIFISCHEN DIAGNOSTIK UND THERAPIE DER TUBERKULOSE F. AERZTE UND STUDIERENDE. VON DR. PANDALLER, Chefarzt des Sanatoriums Schwarzwaldheim in Schömburg bei Wildbad, und Prof. Dr. ROEPKE, Chefarzt der Eisenbannheilstätte Stadtwald in Melsungen bei Kassel. Achte Auflage. Mit einem Vorwort von wirkl. Geh. rat Prof. Dr. R. Koch, Exzellenz. Seite 409. Mit 25 Temperaturkurven auf 7 lithographischen Tafeln, 2 farb. lith. Tafeln und 6 Textabbildungen. Würzburg: Verlag von Curt Kabitzsch.

THE eighth edition of this work undertakes to bring up to date the efforts of previous editions, and to present as far as possible in one volume the various aspects of tuberculin in diagnosis and treatment. The simplicity and clearness in the arrangement of the different subjects is admirable. The references exceed four hundred in number, and are nearly all to German publications.

With all their enthusiasm for tuberculin in diagnosis and treatment, an enthusiasm this work would incline one to believe is widespread and increasing throughout Germany, the authors in many respects show a commendable conservatism. The precautions to be observed in the preparation and application of tuberculin, the proper selection of patients, the association of this with all other available methods to combat tuberculosis, and the limitations of tuberculin, are all emphasized and presented with much detail. While not claiming for tuberculin all the efficacy one could wish is actually possessed, they attribute a very high place to it among the various means at our command. Small initial doses are used in treatment, and reactions are avoided or limited. Albumose-free tuberculin is the form most recommended, supplemented, in proper cases, by Bacillen-emulsion, thereby to produce both a toxic and a bacterial immunity. The author's efforts and hopes have lain chiefly in the production of an active immunity.

It would be a great satisfaction to be able to subscribe to all the claims of this work, which is based on so long and extensive an experience. To properly support any other attitude with full justice to either the authors or the reviewer is impossible within a brief space. The burden of proof, however, lies with the authors. It may be requiring a great deal to ask for greater pathological evidence favoring the value of tuberculin, however important such evidence is, but even the clinical evidence furnished by the

authors is not satisfying. From the large sum of figures available from many sources it is difficult to glean more than a small proportion that carry real weight. One looks in vain in the present volume for figures that are properly comparative, that is, dealing with cases divided as nearly as possible into two equivalent groups, observed under similar conditions, treated alike except that one of the groups receives tuberculin treatment, and followed up for a number of years while living as nearly as possible under similar conditions. Only two years have elapsed since the authors began to use albumose-free tuberculin.

Exception is to be taken to the authors' general statement that tuberculin treatment is indicated in the hands of the general practitioner, or may become so by the pursuit of proper courses of instruction, especially when such treatment by him follows an initial course of treatment of the patient in an institution. The average practitioner has yet much to learn about the available methods of diagnosis of tuberculosis, and of its treatment with non-specific methods more than can be acquired within a brief period of time, as many who have sought special instruction about tuberculosis are willing to acknowledge. But even with the proper equipment for treating with tuberculin, would the average practitioner possess the requisite amount of time to safely carry on the treatment?

C. M. M.

PRÉCIS DE CHIRURGIE DE GUERRE. By E. DELORME, Médecin Inspecteur Général de l'Armée, Membre de l'Académie de Médecine, Membre et ancien Président de la Société de Chirurgie, grand officier de la Légion d'Honneur. Pocket-size octavo with flexible binding. Pp. 218. Paris: Masson et C<sup>ie</sup>.

THIS little book was written hurriedly by Delorme shortly after the outbreak of hostilities. It is based on various observations from recent wars. It consists of twenty-one short chapters in which are described weapons and projectiles, wounds of various tissues, and wounds of various regions, from the skull to the feet; while at the end of the book is a series of specimen charts for recording certain data. It is characterized by brevity and clearness.

Most of the book is a record of first, what tissues do to bullets, and second, what bullets do to tissues: one can find out what a bullet is liable to do to practically every portion of the body. The burning, practical questions of the military surgeon when confronted with a wounded soldier are: What has the bullet done, and what is the best thing for me to do? Working in the field hospital under strenuous conditions the surgeon must rely upon his knowledge of anatomy to find out what the bullet did, and upon his "horse sense"

and judgment to determine what is best for the patient. War surgery differs from civil surgery only in the field; from the base hospital rearward there is no difference. With few exceptions conservatism is the thing in the field; the important question to decide is, How far may the patient be transported with safety?

The statement of MacCormac that "A man wounded in the abdomen dies if operated upon; he lives if let alone," is forcibly supported in the following passage: "In the Transvaal, at Spion Kop, all the wounded, being in a mountainous country, and having necessarily to be transported over very rough ground, succumbed; at Jacobsthal a great many men who were not moved recovered. We have seen quite a series of wounded cured by expectation, the soldiers having been obliged to remain on the field of battle for several days without being able to move from one spot, with nothing to drink or eat."

But little is said about wounds from cold steel; nothing on the value of human blood serum in hemorrhage; while the work antedated, of course, the recent exhaustive observations of Fauntleroy on gas-bacillus infection, as well as the prophylaxis and curative treatment of poison-gas cases.

The book should be of great value if read by one about to enter upon medical military service, for it imparts a good, general working knowledge of military surgery.

P. G. S., JR.

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THE JOHNS HOPKINS HOSPITAL REPORTS (MONOGRAPHS, NEW SERIES, No. VII) VENOUS THROMBOSIS DURING MYOCARDIAL INSUFFICIENCY. By F. J. SLADEN, Resident Physician and M. C. WINTERNITZ, Associate Pathologist, The Johns Hopkins Hospital. Pp. 40; 2 figures; 1 colored plate. Baltimore: The Johns Hopkins Press, 1915.

This monograph is an admirable summary and discussion of cases of venous thrombosis occurring during myocardial insufficiency. To forty-eight abstracts of cases published in the literature are added seventeen unpublished cases, observed mostly in the Johns Hopkins Hospital. Several facts of interest are brought out: (1) Extensive venous thrombosis is commoner than has been believed hitherto; (2) is frequently difficult to diagnose; (3) should be suspected whenever the edema of myocardial insufficiency is asymmetrical; (4) occurs more often in females than in males, but at any age; (5) most commonly follows rheumatic mitral disease. It should be remembered, however, that myocardial degeneration was probably also present in most of the cases diagnosed primarily as valvular. As an "irregular pulse" is frequently mentioned in the abstracts, it would be interesting to know whether such types of cardiac



arrhythmia as auricular fibrillation bore any relation to the incidence of thrombosis. From this point of view, the absence of polygraphic or electrocardiographic records is regrettable. It is also unfortunate that in the more recent cases at least, observation on venous blood-pressure could not have been included, as here also a valuable relationship might have been established. Brödel's three illustrations are, of course, excellent. One would appreciate, however, a more detailed description of some of the features of the colored plate.

E. B. K.

SURGICAL OPERATIONS WITH LOCAL ANESTHESIA. By ARTHUR E. HERTZLER, A.M., M.D., Ph.D., F.A.C.S., Surgeon to the Halstead Hospital, Kansas, the Swedish Hospital, Kansas City, Mo., and to the General Hospital, Kansas City, Mo. Pp. 132; 173 illustrations. Second edition. New York: Surgery Publication Company, 1916.

IN this the second edition, the author has widened his scope and treated the whole general subject of local anesthesia in surgery. He describes in detail the technic of the injection, the drugs employed, their choice and their administration in minutiae. Major and minor operations are described and the special method of anesthesia for such is illustrated.

No attempt is made to theorize as to the production of anesthesia. The work is purely a practical one covering this side of the subject from beginning to end. Emphasis is laid upon the knowledge of anatomy and gentleness in all manipulations and surgical procedures.

The book is very well gotten up in every way, the subjects are well arranged, the illustrations well made, clear and instructive, and the text makes very pleasant and easy reading. It tells one all he desires to know about the practical side of local anesthesia. Many apparently minor points, yet very important points are elucidated, points which have been heretofore inexplicable to the reviewer at least. It is a work I am glad to own.

E. L. E.

POSTMORTEM EXAMINATIONS. By WILLIAM S. WADSWORTH, M.D., Coroner's Physician of Philadelphia. Pp. 604; 304 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

CRITICISM of Dr. Wadsworth's *Postmortem Examinations* must be favorable or qualified, largely as the book is regarded as a monograph *in extenso* or a text-book for students and practitioners. If offered in the latter sense it is impossible, for it should, as a text-

book, set forth facts and principles commonly accepted among pathologists as proven; or, if not as yet accepted, at least a statement to that effect should be made. Contrary to this the author frequently, and often at length, philosophizes upon personal theories not accepted by the pathological world before being submitted as proper text-book matter. Examples to point are the "gastric hair" and "colds in the kidney." Especially to be deplored is the discouragement of orderly and routine methods in performing post-mortems. To one who has performed 4000 autopsies, order may be unnecessary; but to students and occasional obductionists who outnumber the 4000 class 4000 to 1, and for whom the book is supposedly intended, the advice is wrong and rigid adherence thereto unsafe.

Apart from the technical aspect of the book we quote verbatim as follows: "L. died in a hospital of heroin poisoning, and great was the indignation when I pointed to the facial contracture and then cut out an apoplexy" (page 109). And again: "Thirty years ago, while at school, I took pictures, with a sixteen-dollar outfit, that I would be willing to have compared with some that take prizes today" (page 555). An additional space would permit multiplications along similar lines almost *ad lib*. Most certainly the work would make far better reading did not the author go so far out of his way to unnecessarily, uselessly, and indiscriminately "knock" his colleagues (not alone the pathologist, but anatomist, clinician, and general medical literature as well) and keep himself so constantly before the reader. And this applies whether the work be considered as text-book or monograph.

The photographs are uniformly excellent, and by them the author has shown himself the consummate artist and skilled technician; many original devices are shown from time to time indicating real mechanical genius, and the part on medico-legal postmortems brings out many valuable points. But beyond these latter it is difficult to go.

F. S. W.

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THE DUCTLESS GLANDULAR DISEASES. By WILHELM FALTA, Vienna. Translated and edited by MILTON K. MEYERS, M.D. Pp. 658; 101 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

If anyone still doubts the truth of the old saying that words are given to man to hide his thoughts, let him borrow the American edition of Falta's work and spend an evening with it.

As a whole the book is a valuable collection of material concerning all phases of the disorders of the ductless glands, and over sixty pages of references to the literature evidence its painstaking preparation. However, our knowledge of the ductless glands today does

not lend itself to finished presentation, and much confusion and contradiction is still inherent to the subject. This complexity is made worse by the author's style, which is unpardonably verbose and discursive, and renders the reading of the book a very doubtful pleasure. Its value to the average reader is uncertain, for it does not pay to work an ore of less than a certain percentage of gold to the ton, and in the reviewer's opinion the gold in the ore in this instance runs perilously low.

But whatever our estimate of the work in the original German, there can be no doubt of its greatly lessened value in the American edition, for in the translating and publishing many further difficulties for the reader have been introduced.

To him, however, who decides to dig in this American edition can be promised some precious gems of careless proofreading. Every few pages the tedious text is enlivened by a sentence the meaning of which has been beclouded by the substitution for the original of a word similar in appearance if not in meaning; thus confer instead of compare (page 89), proves instead of paves (page 51), and placed instead of played (page 36). Similarly can be explained such enlightening statements as: "On account of the marked excretion of sweat, malaria sometimes occur" (page 82), and "The diagnosis made was congenital abscess of the uterus . . ." (p. 438), while the legend to an illustration on page 577 gives a unique translation for "Fettgewebes." It reads, "Inflammatory alteration of the feet-tissue in a case of adipositas dolorosa." Grammar is often ignored and the verb is, as a rule, firmly entrenched at the end of each sentence. The spelling is good except in personal names thus: Hayem is met as Hajem, Morawitz as Morowitz, and C. v. Noorden as C. V. Noorden.

Naturally one's sympathy is aroused for the author whose work has been published for American readers in such a slipshod manner, and one is also a little sorry for the readers, but they at least are free agents, and have the cure for such publications in their own hands.

O. H. P. P.

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HYSTERIA AND ACCIDENT COMPENSATION, NATURE OF HYSTERIA AND THE LESION OF THE POST-LITIGATION RESULTS. By FRANCIS X. DERCUM, M.D. Pp. 120. Philadelphia: The Geo. T. Bisel Company, 1916.

THIS short essay on hysteria and accident compensation is apparently intended for the legal profession and as such it presents the subject very well. The author believes that in most instances in which nervous conditions follow accident that the symptoms are largely and in most cases altogether the result of the litigation and that as soon as the litigation is ended all symptoms disappear.

He quotes largely from the German and other literature and from his own very large experience. However, while most neurologists will not agree with this point of view, nevertheless, Dr. Dereum's presentation from this standpoint is a very good one.

T. H. W.

LEGAL PRINCIPLES OF PUBLIC HEALTH. By HENRY BIXBY  
HEMENWAY, A.M., M.D. Pp. 859. Chicago: Flood.

This publication is surely, as is stated in the introduction, a sign and product of the times. We are slowly coming to a realization of the importance of public health work, as is evidenced by the fact that a large percentage of our communities are becoming interested in a manner demanding recognition. The sentiment of the populace, as their education in public health problems advances, is strongly in favor of employing men especially trained in this branch, or, perhaps better, specialty of Medical Science.

The subject matter might be, in some respects, adversely criticized, but the whole work is so excellent that such criticism would seem unwarranted.

The scientific basis of public health work is discussed briefly and clearly. There is one point in this chapter which must be criticized, namely, the interpretation of Koch's postulates. These postulates, as originally formulated by Koch, have been variously modified by different authors, in some instances so greatly that their identity is practically lost.

The different chapters deal with the various phases of the legal aspect of public health questions in as nearly as possible a systematic manner.

The chapters on due process of law and nuisance are followed by public health powers and limitations. After reading and mentally analyzing these three interesting chapters, one is forcibly impressed with the fact that "limitations" are a serious handicap to those who are endeavoring to protect the health of our communities.

The various phases of public health administration are very ably dealt with. Quarantine is considered in some detail. The prevention, legal and commercial aspects are clearly discussed.

The reader is at first impressed with the brevity of the chapter on water supplies, drainage, pure food, and drug regulations; however, on analyzing them carefully, it will be found that the first is excellent, but that the discussion of drug regulations is hardly adequate. It is to be regretted that the work was published before the passage of the Harrison Act.

The last three chapters deal with subjects which are attracting special attention at the present time, namely: industrial regulations, school inspection, and eugenics. Those who have become, as it were, hysterical over the eugenic propaganda, and have carried

their ideas to a point which would lead one to presuppose that they were not themselves absolutely free from mental abnormalities, might well ponder over the last paragraph (512) in the book, which states: The foregoing (*i. e.*, the chapter on eugenics) clearly illustrates that all laws on the subject of eugenics should be based upon the science of biology, no sociologist should attempt to force such legislation without its approval by competent biologists; no legislation is safe upon the subject unless it is reasonable; and to be reasonable it must be grounded on fact, rather than theory; upon science, rather than emotions.

It would seem to the reviewer that this work is an essential in the library of all physicians and officers dealing with public health problems. It contains much valuable information, and the subject matter is treated in such a manner as to make of it exceedingly interesting reading.

N. G.

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A TEXT-BOOK OF NERVOUS DISEASES, FOR STUDENTS AND PHYSICIANS. By ROBERT BING, M.D. Translation by CHARLES L. ALLEN, M.D. Pp. 481; 111 illustrations. New York: Reiman Company, 1915.

BING's work on nervous diseases is of course very well known and it was a happy thought which led to the translation by Dr. Charles L. Allen, who did his work very well. Instead of the usual method of discussion the author subdivided the subject into lectures. For example in his lecture on multiple sclerosis which is typical, he first gives a definition of the disease, then gives a paragraph in which he discusses the pathology, then a longer discussion on etiology and an ample discussion of the symptoms. After this, the atypical forms of the disease, then the differential diagnosis, prognosis, and lastly treatment. This is the plan adopted throughout the book. As can be seen from this it is the logical manner in which any subject would be presented in a lecture and is different from the usual text-book presentation.

The classifications which the author adopts are very interesting. In dyskinesias he includes all forms of tremor, spasms and coarse movements, even including chorea, athetoid movements, paralysis agitans and myasthenia gravis. From the standpoint of the student this is admirable, but from the pathological point of view, as of course the author would willingly acknowledge, such a classification is not probable. The discussion of the syphilitic diseases of the central nervous system is excellent and is as good as can be found in any text-book with the exception that the treatment is necessarily just a little out of date inasmuch as the original book was published several years ago. The lecture on arteriosclerosis of nervous centres is the best that the reviewer has read in any book, as is also the chapter on aphasia, apraxia, and agnosia. The

lecture on tumor formations is disappointing in the sense that it is not large enough and leaves a good deal to be desired. The discussion and classification of what Bing terms dysglandular symptom complexes is excellent. He includes in this Basedow's disease, myxedema, Addison's disease, and dyspinealism. His lecture on the sympathetic and trophoneurosis leaves nothing to be desired. The illustrations are excellent and far better than what is found in most text-books on nervous diseases. The diagrams, most of which are taken from his compend, are also excellent. Altogether it is one of the best and most satisfactory works on nervous diseases that has appeared for some time, and is far better than some of the more recent books by American authors. From the point of view of the student it is in the reviewer's mind the best work that has appeared for many years. T. H. W.

SEROLOGY OF NERVOUS AND MENTAL DISEASES. By D. M. KAPLAN, Director of the Clinical and Research Laboratories in Neurological Institute of New York. Pp. 346.

THIS volume confines itself entirely to the serology of nervous and mental diseases and practically to those dependent upon syphilitic infection. It is the first collected study of these reactions appearing in English, and fills a unique place in the library of clinical tests.

Kaplan divides the book into four parts. The first deals with the technic used in collecting blood specimens, making spinal punctures, and with the description of the methods used in the actual performance of the various tests: Wassermann reaction of blood and spinal fluid; gold solution; globulin reactions; spinal-cell counts, and the reduction of Fehling's solution. These tests are so briefly and adequately described that anyone at all familiar with the serological technic could easily follow them. The second part deals with the serological findings in the various mental and nervous diseases using these five tests. Beginning with the diseases of the meninges, he gives the formula in practically every involvement of the central nervous system. The third part confines itself to syphilitic diseases, describing in detail every combination of findings in cerebrospinal syphilis, tabes, and paresis, with the average changes occurring in these formulas under successful treatment. The fourth part deals with the preparation and the technic of administration of salvarsan.

The book fills a real need and as a text-book is equally valuable to the general practitioner, neurologist, and laboratory worker. One can not but regret that it is so definitely limited to syphilis and that some of the other serological tests are not included.

S. D. W. L.

# PROGRESS OF MEDICAL SCIENCE

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## MEDICINE

UNDER THE CHARGE OF

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**The Urochromogen Test in the Urine in Typhoid Fever.**—V. SVESTKA (*Wien. klin. Wochenschr.*, 1915, xxviii, 1054) has studied the urochromogen test of Weiss and the diazo test of Ehrlich in a series of cases of typhoid fever. He found both tests positive in all of 52 cases of typhoid fever and 3 of paratyphoid fever. In 26 cases of suspected typhoid, all of which remained negative bacteriologically, each test was positive in one case only. Each test was also positive in only one of 45 healthy individuals vaccinated against typhoid fever. The author performed the test as Pulay described it, except that he diluted the urine till it was colorless; only an intense canary yellow color was looked upon as positive. The urochromogen test was positive in the first week of typhoid fever. The bacteriological diagnosis in the cases studied was positive during the second week.

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**Anaplasma like Bodies in the Blood of Vertebrates.**—ANNIE PORTER (*Ann. Trop. Med. and Parasit.*, 1915, ix, 561) calls attention to the fact that many papers have been written during the past ten years dealing with blood parasites occurring in the blood of vertebrates, and points out that some papers would have been much improved by a careful preliminary study of the elements of apparently normal blood, or of blood under definite pathological conditions. By such a study a number of so-called "parasites" would have been found to be artefacts or reaction products and not true organisms. She particularly calls attention to the fact that this is probably true of the bodies called by Theiler "anaplasmata" and considered by him to be the cause of "gall sickness" in cattle in South Africa. In the present study the

author has examined the blood of a number of vertebrates and has compared them with specimens taken from South African cattle and blood from obscure cases of human anemia. Viewed in the fresh, anaplasma appear as small rounded granules without morphological differentiation within the erythrocytes. They usually are single, but forms apparently dividing may be seen. They show no differentiated structures by intra-vitam staining. In stained preparations these structures are usually round, rarely irregular and take a deep chromatin or basophilic stain. Forms resembling diplococci are not uncommon. The author comes to the conclusions reached by a number of others, which is to the effect that the so-called "anaplasma" are not protozoa but that they represent a product of the degeneration of the red cells due to the action of some vital substance or substances in the host. They occur in healthy and anemic vertebrate bloods, both warm and cold blooded. The author is of the opinion that probably these bodies are of nuclear origin.

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**A Test for Urobilin in Urine and Feces.**—A. EDELMANN (*Wien. klin. Wochenschr.*, 1915, xxviii, 978) describes a modification of Schmidt's urobilin test which is applicable to both urine and feces and which is much quicker than the original test. Instead of a saturated aqueous solution of bichloride of mercury he employs a saturated alcoholic solution; the latter contains about twice as much bichloride as to the aqueous solution. The technic for applying the test to the urine is as follows: Two reagents are necessary: (1) a concentrated alcoholic solution of bichloride of mercury; (2) a 10 per cent. alcoholic solution of zinc chloride, and amyl alcohol; about 10 c.c. of urine in a test-tube are treated with half the volume of concentrated alcoholic sublimate solution, mixed, and then shaken with amyl alcohol (which is best accomplished by pouring the contents down the wall of a second test-tube several times.) To the clear amyl alcohol layer which quickly separates above, several cubic centimeters of the alcoholic zinc chloride solution are added; or the amyl alcohol may be poured into another tube and treated with zinc chloride. With large amounts of urobilin the amyl alcohol is saturated with the pigment and shows a beautiful rose red color (only with pathological amounts of urobilin) and the addition of zinc chloride produces an intense green fluorescence. With small amounts of urobilin, if the fluorescence is not visible with diffuse light, the light may be focussed on the tube with a convex lens, or the light from a small electric flash may be employed. By this means traces of urobilin may be detected. In applying this test to the stools, several grams of feces are rubbed in a mortar with a very small amount of water. Then an excess of reagent I is added, and rubbed a minute longer and filtered into a clean test-tube. To the filtrate, which is red in the presence of urobilin, the addition of a few cubic centimeters of solution II causes a green fluorescence.

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**The Sterilization of Fluids by Means of Animal Charcoal.**—R. KRAUS and B. BARBARA (*Wien. klin. Wochenschr.*, 1915, xxviii, 1031) have previously shown that animal charcoal adsorbs typhoid and



cholera bacilli from water, so that the water may be bacteria-free after one hour. Further experiments have shown that this result may be accomplished in a much shorter time. Thus, 100 c.c. of distilled water, 1 gram of animal charcoal +  $\frac{1}{100000}$  loop of cholera culture per cubic centimeter were shaken together. After fifteen minutes 1 c.c. of the filtered fluid was placed upon agar plates. After twenty-four hours the plates were sterile. With typhoid bacilli they found it necessary to use three to four times as much charcoal to make the water sterile. They have used this method in an attempt to sterilize milk and found that 100 c.c. of milk bought in the market, when shaken with 3 grams of animal charcoal and allowed to stand fifteen minutes, can be passed through a filter paper and recovered bacteria-free. For the sterilization of serum the method has also proved useful. Anti-agglutinins, for example, are not adsorbed by charcoal, as are toxins. Antidiphtherin serum loses none of its potency when treated in this way, though there is a loss in filtering through bacteriological filters.

**Spontaneous Agglutination of the Erythrocytes in Malaria.**—R. BIGLIERI (*Wien. klin. Wchnschr.*, 1915, xxviii, 1054) had his attention called to the fact that red blood corpuscles in malarial blood frequently clump on the slide when a preparation is made by the Ross thick drop method. This phenomenon has not been observed with normal blood. Mornaco and Panici have described an agglutination which occurs when the serum from malarial patients is mixed with human corpuscles. French observers have also noted an agglutination of the erythrocytes in patients suffering with trypanosomiasis. The author examined the blood of 600 patients ill with malaria and 158 of the specimens showed agglutination of the red blood corpuscles in the thick drop. This spontaneous agglutination was found with equal frequency in tertian and quartan infections and somewhat oftener in estivo-autumnal. In 54 cases which exhibited symptoms of malaria, in whose blood no parasites could be found, agglutination was also observed. Spontaneous agglutination of the erythrocytes was also found in septicemia and in pregnancy. The cause of the agglutination has not been discovered.

## SURGERY

UNDER THE CHARGE OF

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**A Simple Operation for Femoral Hernia.**—BRUNZEL (*Deutsch. Ztschr. f. Chir.*, 1916, cxxxv, 67) says that, as a rule, the chief obstacle to the complete closure and removal of the femoral canal is the very tense and

rigid overlying Poupart's ligament. The only simple way of overcoming this tension is to divide the ligament. This can be done, without disturbing important anatomical relations, over the iliopsoas muscle. Brunzel first tried this method toward the end of 1914, in a case of strangulated femoral hernia, and since then in over a dozen other cases, some with very large femoral hernie and all with good results. An incision along Poupart's ligament gives a free exposure of the parts and permits a certain diagnosis between an inguinal and femoral hernia and the opportunity of operating on whichever is found. The sac of the femoral hernia is isolated, opened, its contents reduced, the sac ligated at its neck and cut away. The stump is pushed upward into the abdomen by the finger and the femoral canal freed of fat. A vertical incision is now made through the aponeurosis of the external oblique, including its lower border or Poupart's ligament, over the iliopsoas muscle. Poupart's ligament can then be pressed inward at the site of the femoral canal, when it will hold this position almost without further aid. A few silk sutures are inserted to assure its closure, beginning medially and attaching the lower border of the ligament to the periosteum of the pubic bone and the pectineus fascia and muscle, care being taken not to injure the femoral vessels in their sheath. The cut margins of the external oblique are sutured to the underlying iliacus and internal oblique muscles. The abdominal wall is not weakened by this cutting of the external oblique.

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**The Surgical Treatment of Gunshot Wounds of the Chest.**—DAVIES (*Lancet*, January 29, 1916, p. 232) writes concerning his experiences at the Third London General Hospital and the University College Hospital, his colleagues at the latter hospital allowing him to see and to treat all the cases suffering from wounds of the chest admitted to the military wards. The number of cases of hemothorax was very large and the previous experience so small that this lesion was of great interest. It is rarely possible to recognize the source of bleeding when it is in the chest or lung. The blood in the pleural cavity may be mainly fluid or a massive clot; it may be complicated by the presence of gas or a serous effusion or by infection. Extensive clotting occurs chiefly in shell or shrapnel wounds, from the extensive laceration exposing the blood freely to the action of the tissue ferment and to fragments of rib, or the introduction of portions of clothing. The blood of a hemothorax when caused by a penetrating bullet wound is mostly fluid. In the majority of these cases there is a deposit of fibrin, the amount varying in different patients. Early and, if necessary, repeated exploratory puncture is essential to the successful treatment of these cases. Without it it is not possible to differentiate in the majority of cases between a simple pleural effusion, a hemorrhagic effusion, a fluid hemothorax, a clotted hemothorax, or at times an infected hemothorax. A small quantity of fluid blood may be rapidly absorbed. Larger quantities, a pint or more, must take longer, the rate of absorption varying greatly. Davies advocates the complete removal of the fluid blood by his "oxygen replacement" method. The intrapleural pressure recorded continuously by a manometer is under absolute control. The oxygen replaces the fluid as it is withdrawn and prevents the development of a high negative pressure, which is the cause of all the

danger and distress. Clotted but uninfected blood, requires an opening in the chest wall with the removal of about 5 cm. of rib. If there is no evidence to suggest infection the wound is closed in layers to prevent leakage of air. The air admitted during the operation is replaced by oxygen as above. An infected hemothorax must be drained freely by removing a portion of a rib. The removal of foreign bodies from the lung should not be undertaken unless they are producing definite symptoms which are likely to be progressive, and even then the operation should not be done until the initial reactionary inflammation has subsided.

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## THERAPEUTICS

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UNDER THE CHARGE OF

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**The Intraspinal Treatment of Syphilis of the Central Nervous System According to the Method of Swift and Ellis.**—DEXTER and CUMMER (*Arch. Int. Med.*, 1916, xvii, 82) have given 59 intraspinal injections of autosalvarsanized serum in 10 cases. Following these injections, they have seen no symptoms, temporary or permanent, which could in any way be attributed to injury to the central nervous system. There have been no deaths, paralysis, or bladder disturbances. Two of the patients have experienced no discomfort from the procedure. When gastric crises or lancinating pains exist, attacks of pain, in all ways similar to the preëxisting crisis are apt to follow the injections. These crises usually follow the treatment after an interval of from two to four hours and they are often very severe. Their duration is usually short, and they are followed by much increased periods of freedom from pain. As the treatment continues these postoperative attacks become less and the spontaneous crises often disappear entirely. It is of interest to note that those patients who have had these reactions of pain following the treatment have shown greater and more rapid improvement than those who had no discomfort from the procedure. The authors found that the increased globulin content in the spinal fluid is very resistant to treatment. The pleocytosis disappears rapidly. Their experience has been that the Wassermann reaction in the spinal fluid is the most difficult of the laboratory findings to influence. The reaction often persists in the larger doses of spinal fluid, long after the other laboratory findings have come within the normal limits. The changes in the physical findings have been a partial or complete disappearance of disturbances of sensation, lessening or disappearance of ataxia and a marked increase in weight and strength. In no case have absent deep reflexes returned, and no change in papillary reactions have been observed. The abatement or disappearance of symptoms has been most striking. In every

instance in which lancinating pains were present, they have either disappeared completely or have diminished so much that they have ceased to be a real annoyance. Gastric crises and vesical incontinence have also been favorably influenced. The results in 6 of these 10 cases have been a symptomatic improvement so emphatic that the patient's economic efficiency has been restored. They are able to work and to enjoy life to all intents and purposes as normal individuals. They feel that the best results will be obtained in cerebrospinal lues, and in tabes of the early or moderately advanced types. In far advanced tabes the results are in most cases dubious to say the least. Their own experience with paresis is too limited to make any generalization. It seems probable to them, however, that very little can be done to improve permanently a paresis once it is well established. In concluding, Dexter and Cummer feel that they can state fairly that the Swift-Ellis method is safe when the original technic is followed out to the letter. The claim of the originators that it is a valuable adjunct to the treatment of syphilitic involvement of the central nervous system is sustained as far as tabes dorsalis and cerebrospinal syphilis are concerned. It is a method which is not essential in all cases, but which applied carefully and controlled intelligently will bring about definite amelioration in symptoms and in laboratory signs where other accepted modes of attack have failed.

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**Mercury Elimination in Bichloride Poisoning.**—Vogel and Lee (*Med. Record*, 1916, lxxxiv, 58) have found that the elimination of mercury in cases of acute bichloride poisoning may continue for periods of time ranging from a week to several months, and treatment should be continued until it has been shown that elimination of the drug is ceasing. The excretion usually continues longest from the bowel and systematic flushing of the large intestine should always be carried out, but the gastric mucosa and the skin are also important as channels of elimination and should be utilized in order to spare the renal epithelium.

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**The Nature of Liquid Petrolatum.**—Brooks (*Jour. Am. Med. Assn.*, 1916, lxxvi, 24) says that although the crude petroleum obtained from the world's various producing districts vary greatly in composition, the refined oils intended for internal administration are essentially of the same composition. Hence there can be no different therapeutic effect obtained from the Russian variety than from the American. He notes that the internal use of the lighter oils, lighter than the specific gravity of 0.885 is to be condemned owing to the fact that annoying leakage is much more common with the lighter oils. Leakage will rarely result if only the more viscous oils of 0.885 specific gravity or heavier, be employed for internal use. The important tests in order to determine the suitability of various preparations of liquid petrolatum are undoubtedly taste, keeping quality, and viscosity. The specific gravity is roughly a measure of the viscosity and it may be substituted for the viscosity determination. One of the most important tests to make is for keeping quality. Many oils are perfectly colorless and tasteless when freshly prepared, but after standing, particularly if exposed to the light, acquire an objectionable taste and a light green color. Exposure to daylight in loosely stoppered bottles

will develop very marked differences in oils which originally are excellent in quality, within from four to ten days. The author has found that masticating the oil with ordinary white bread will bring out any petroleum taste that may be present. This test is very delicate and makes it possible to eliminate oils with this objectionable taste. Brooks does not believe that various chemical tests that have been proposed to test the purity of liquid petrolatum are of any value whatever. He believes that the simple tests he has suggested are easily sufficient to determine the relative merits of different oils. The freezing test for detecting the presence of paraffin has also been proposed; but if paraffin does not separate from the oil at room temperature, it certainly could not do so in the body. The presence of a small amount of paraffin indicates that the oil has probably been prepared from one of the so-called "paraffin base" crudes, and does not indicate an adulteration.

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**Sodium-salvarsan.**—WECHSELMANN and DREYFUS (*Münch. med. Wchnschr.*, 1915, lxii, 177, 178) report their clinical tests of a new salvarsan preparation given them by Ehrlich for trial. This preparation is called sodium-salvarsan and chemically is practically the same in fixed form as is obtained by adding alkali in the preparation of solution of salvarsan for intravenous injection. Their experience with this new preparation extends over a period of one and a half years. They both recommend it very highly on the ground that it has the same clinical action as the original salvarsan while it is readily soluble and therefore lends itself easily to intravenous injections. Sodium-salvarsan contains about 20 per cent. of arsenic and is a yellow powder which darkens on exposure to air and becomes insoluble and very toxic, hence it must be used in fresh solution as is the case with neosalvarsan. Solutions of sodium-salvarsan are alkaline and for that reason they are not to be recommended for intramuscular use. Both authors recommend the giving of sodium-salvarsan in doses of from 0.3 to 0.6 gram, two or three times a week. They have given in certain cases as high as forty and even fifty doses, but as a rule, from 4 to 7 grams are sufficient. They say that sodium-salvarsan injections give rise to fewer reactions than either of the other two forms of salvarsan. Wechselmann says he uses it freely in a great many conditions in which previously it was considered risky to try salvarsan therapy. He mentions among such complications chronic nephritis, optic neuritis, etc., and says that in certain cases he has noticed that albuminuria has improved following the use of sodium-salvarsan. Wechselmann considers that it is very important to use pure salvarsan therapy as he believes that the combined treatment has a tendency to increase the toxicity of the salvarsan to the danger point. He also does not approve of giving sodium salvarsan in concentrated solution by a syringe but prefers to give it in a solution, using 10 c.c. of a 0.4 per cent. salt solution for every 0.1 gram of the drug. Dreyfus, on the other hand, prefers to give it in concentrated solution in distilled water by means of a glass syringe, the total amount of fluid being about 30 c.c. He also strongly favors the combined treatment, using two doses of sodium-salvarsan and one of mercury per week. They both claim that sodium-salvarsan combines the more intensive action of salvarsan on syphilis with the simple technic of neosalvarsan.

**An Experimental Study of Lavage in Acute Carbolic Acid Poisoning.**—MACHT (*Johns Hopkins Hosp. Bull.*, 1915, xxvi, 98), on the ground of experimental work on animals, says that the efficiency of lavage in phenol poisoning depends on the quantity of poison taken, on the time after poisoning that the lavage is begun, and in the solution used for washing the stomach. A strong solution of sodium sulphate appears to be the most useful for the purpose; next in efficiency comes plain water. The influence of alcohol in phenol poisoning depends on the time of its administration. An animal that is previously intoxicated with alcohol can withstand better the effects of phenol taken afterward. On the other hand, alcohol administered to an animal after poisoning with phenol will aggravate the symptoms and hasten death. The use of alcohol in carbolic acid poisoning should therefore be strongly discouraged.

## PEDIATRICS

UNDER THE CHARGE OF

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**Vascular Diseases in the Young.**—CHARLES W. CHAPMAN (*Brit. Jour. Child. Dis.*, 1916, xiii, 97), in reviewing this subject, shows that arteritis is not infrequent in infancy and adolescence. This condition affects normal development and tends seriously to shorten life. From a large number of reported cases it would appear that inherited syphilis is probably the basic factor in the majority of cases although the condition is also caused by infectious diseases such as rheumatic fever, diphtheria, scarlet fever, pneumonia, and tuberculosis. Among the reported syphilitic cases are aneurysm of the abdominal aorta in a fetus of eight months and seven cases of thoracic aortic aneurysm under ten years, many of them associated with arteritis. Thickened and tortuous arteries, often with ventricular hypertrophy and accentuated second aortic sound were found in toxemias, such as intestinal or nephritic in children under the age of puberty. Under proper treatment most of these signs disappeared. Numerous cases of calcification of the aorta and peripheral arteries are recorded in infants as young as six months and in children. Not all of these were due to syphilis. After a detailed account of four cases of arteritis in infants and young children, three of which were due to syphilis, the author discusses the diagnosis, prognosis and treatment. Under the first, arterial thickening should be looked for in the brachial and femoral arteries besides in the radials. Arteritis causes swelling and pain in the affected limb and aortitis shows a diminished resonance over the manubrium. History of syphilitic infection, stigmata or a positive Wassermann reaction are important factors. Arteritis due to toxemia from overfeeding or from the intestines usually improves under mercurial purges. The treatment is that of the infection causing the arteritis. Fixation and moist heat

for involved limbs, mercurial purges and correcting dietetic errors in intestinal toxemia and appropriate treatment in syphilitic cases are called for.

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**The Prevention of Respiratory Disease in Early Life.**—ROYAL STORRS HAYNES (*Arch. Pediat.*, 1916, xxxiii, 81) emphasizes the fact that respiratory diseases in early life have not been diminished as have intestinal diseases. The infectious cold is most vicious probably in its sequelæ and complications and in its attendant lowered vitality which encourages other diseased conditions. The first five years of life are particularly susceptible partly on account of the effects of rickets, measles, pertussis and adenoid growths. Also the narrowness of the respiratory passages plays an anatomical part. Lowering of resistance is the primary cause and is brought on usually by exposure to cold, fatigue, auto-intoxication, poisoning by food or chemicals. Among the factors to be overcome is the dust nuisance. Oiling and watering of streets tends to prevent outdoor dust. Vacuum cleaners, dustless dusters, wet-sweeping and the use of rugs instead of carpets is desirable. The smoke of large cities is an irritant and should be minimized as it markedly increases respiratory diseases. Crowding in houses, street cars, trains, theatres, etc., is a great factor and its elimination tends to control a large part of respiratory diseases. The regulation and control of measles and pertussis, especially the early recognition and isolation of cases, the isolation of susceptible contacts and increased control in the reporting of cases would cut down the respiratory conditions attending these diseases. Regulation of attendance at school of children with respiratory affections is important. There is no such thing as a "little cold." "Open air" schools and "open window" schools minimize respiratory conditions. Proper care of children in the home through hygiene and sanitary measures, to keep up the resistance of the child is the most important prophylactic measure. Personal hygiene and the factors of food, clothing, ventilation, sleep and bathing are all important. The proper hygiene of the mouth is important as bacteria grow well there. The destruction or exclusion of the infecting organism and the preservation of resistance of the individual especially are the most important factors.

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**Mitral Stenosis in Young Children.**—MURRAY H. BASS (*Arch. Pediat.*, 1916, xxxiii, 107) describes two cases of mitral stenosis in children, one in a boy of ten years, with no etiologic factor except a normal case of measles, recognition of the condition at the sixth year, no symptoms referable to the heart and a negative Wassermann and von Pirquet. However there is marked stunting of growth and a mentality below normal. The other case, of a boy, seven and one-half years old, had cervical adenitis, has had scarlet fever mildly, showed a positive Wassermann, and was markedly under-developed and puny. The only signs of a cardiac condition were occasional attacks of cough and dyspnea. Antisyphilitic treatment caused an improvement in his general condition and appetite and his cervical adenitis, his weight and stature practically remaining the same during almost two years following. The lack of development shown in both these cases is due presumably to the cardiac disease. In mitral stenosis in children

where no signs of insufficiency are present, syphilis should be thought of and a Wassermann done. Cardiac disease, especially valvular stenosis exerts a considerable influence on growth. From the literature on this subject one concludes that mitral stenosis has been observed at autopsy in infants; that it has been observed in children over five years old with no apparent etiological factor present though without sufficient evidence of their being "congenital"; no case of mitral stenosis has been found reported in children between the ages of infancy and five years. Weber suggests that in the small size of the body in these cases one sees a "conservative adaptation or conservative hypoplasia of the whole body—nature's attempt to limit the growth of the patient in accordance with the limited blood supply."

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**Treatment of Scarlet Fever with Fresh Blood from Convalescent Patients.**—ABRAHAM ZINGHER (*New York State Jour. Med.*, 1916, xvi, 112) reports the results of injecting fresh blood from convalescents into the muscles of scarlet fever patients. This method for the intramuscular injection of whole blood represents a convenient way of giving a patient human serum. The following muscles are chosen and a syringe-ful (one ounce) of blood is injected into each place: the gluteal regions, the outer regions of the thighs, the calves and the triceps muscles. The blood is taken from the median cephalic vein of the donor. From four to eight ounces of blood are taken. Absorption from the muscles takes place rapidly and usually without further local irritation. Fourteen cases of toxic scarlet fever were injected. They were selected out of 650 admissions on account of the severity of symptoms. Of the 14 cases 4 died, being almost moribund on admission. The amount of blood injected varied from 75 c.c. to 250 c.c. Larger quantities, from 8 to 10 ounces have been found to exert a distinctly beneficial effect in some very septic late cases. The effect of the blood in the 10 recovered cases was as follows: Some of the cases showed a very definite relationship between the injection and a critical drop in temperature with improvement of the circulation, general condition and especially mental condition. The reaction begins from two to four hours after injection and is completed in nine to fourteen hours. It has no effect on secondary septic conditions. The pulse becomes stronger, steadier, and slower. Cardiac symptoms and the cyanosis improve and respiration becomes more normal. General condition improves perceptibly and subjective symptoms disappear. Rash fades rapidly. If any benefit is to be derived from convalescent blood its action must be brought into play early, before toxemia is overwhelming. Addresses of convalescents can be kept on record and donors in this way may be sent to private homes. Considerably more therapeutic work of this kind must be done before definite conclusions as to the value of this treatment can be made.



## OBSTETRICS

UNDER THE CHARGE OF

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**The Aseptic Care of the Umbilicus in the Newborn.**—MÜLLER (*Ztschr. f. Geburts. u. Gynäk.*, 1914, lxxvii, 3) reports the results of methods employed in the hospital at Basel, Switzerland, in the service of von Herff. The material included 4000 newborn children. He concludes that it is impossible to escape a typical surgical aseptic process in the healing of the umbilical wound. He believes that this region becomes infected in the child's passage through the vagina and that one can distinguish the line of demarcation between necrotic tissue and connective-tissue which is undergoing mummification. All that one can do then in the interest of the child is to protect it against the most pathogenic and virulent bacteria. For this purpose, the ordinary daily bath is omitted. The umbilicus after its first dressing remains undisturbed for ten days, unless a foul odor, excessive secretion or fever develop. The child's body may be sponged and cleanliness maintained without disturbing the umbilicus. The results of this method are the rapid granulation of the umbilicus with a minimum of cases of infection. The stump of umbilical cord affords especially desirable material for the growth of bacteria. The tissue is rich in water and gelatinous in composition. To avoid trouble, the cord should be cut as short as possible, the stump crushed and so dressed as that air can gain access freely during the process of healing. The granulation tissue at the umbilicus is exceedingly sensitive to chemical and mechanical irritation. All forms of dressing or applications should be so applied as to make the least possible irritation. The method used in the Basel Clinic is as follows: As soon as pulsation ceases in the umbilical cord, which should inevitably be waited for except in cases of operation, or where immediate necessity is present, the cord is ligated 8 cm. from the umbilicus with linen tape 0.5 cm. broad with double ligature and then is severed. The cord must not be touched by the midwife or physician except with hands thoroughly disinfected with alcohol or with sterile material. As soon as the child is taken to the nursery for its initial bath von Herff's clamp is applied. This instrument is shaped like a hemostat with jaws considerably longer, serrated and bent at an angle. The instrument weighs 12 gms. It is applied very slowly upon the stump of cord so that the vessels are not torn and thus hemorrhage afterward is prevented. The clamp is applied close to the skin. The vernix is removed with sterile olive oil, the clamp removed and the cord tied close to the skin at a point where the cord has been thoroughly compressed by a ligature. The child is then bathed and the cord cut close to the ligature. The umbilicus is dressed with a sterile round compress of muslin kept in position by an inherent ring. This dressing remains undisturbed for ten days. In experimenting various substances were tried and the effect noted. Thus: balsam of Peru,

thymol in alcohol, thymol in vaseline, noviform, sugar and hydrogen peroxide were all tried. Of all the materials employed, balsam of Peru gave the best result; sugar next; 10 per cent. noviform salve without cotton next; and hydrogen peroxide last. Among the material observed, were four cases of umbilical infection. All of them were mild in character and speedily disappeared under applications of alcohol. In reviewing the results of the clinic showed that in the last 5000 children treated from 1912 to 1914, there was no case of umbilical infection. In prior years, the mortality from this condition was estimated at 0.07 per cent. in 10,000 children.

**Rupture of the Uterus During Pregnancy.**—MEYER (*Arch. mens. d'obstet.*, August, 1915) reports three cases of rupture of the uterus during pregnancy. The first was in a woman, aged thirty-five years, who had had nine pregnancies previously, three terminating prematurely. About six weeks before term, the patient was suddenly seized with prostration, abdominal pain, the discharge of a little fluid from the vagina and the development of shock. When brought to hospital, the patient was without appreciable pulse, the abdominal condition could not be clearly made out by palpation but the abdomen was immediately opened. There was a large quantity of blood in the peritoneal cavity, the fetus was in Douglass's pouch. The body of the uterus had ruptured from above downward near its left border and at the point of rupture had become inverted. Hysterectomy was practised but the patient succumbed. An examination of the uterus could assign no cause for the accident. The second patient was a multipara who came into labor with inefficient uterine contractions. The abdomen was greatly enlarged, exceedingly painful on palpation. A physician who was summoned administered morphin and chloral but the hemorrhage continuing, the patient was brought to hospital as a case of placenta previa. On admission, her clothing was soaked with blood and Moneberg's bandage was immediately applied, arresting the hemorrhage. While the patient was being prepared for abdominal section, she died. Autopsy showed a longitudinal rupture in the body of the uterus near the right border. Examination of the uterus failed to reveal any histological changes in its substance. His third case (also a multipara) who had had no labor pains but who, upon going to a toilet, was suddenly taken with severe abdominal pain. The patient was pale with a very feeble, regular pulse, the abdomen very painful upon palpation. The urine contained albumin and casts, there was no hemorrhage nor uterine contraction. Morphin was given to relieve pain, but the symptoms continued and the patient gradually grew worse. On opening the abdomen, there had been considerable hemorrhage with rupture at the fundus. The child was living but died shortly after birth. The mother made a tedious but complete recovery.

**The Causes Which Stimulate the Mammary Secretion During the Puerperal Period.** ZULOAGA (*Arch. mens. d'obstet.*, September, 1915) has studied the factors which stimulate the secretion of milk. He describes the case of a patient pregnant about four months threatened with abortion in whom he used a tampon of gauze. The patient had strong uterine contractions and on removing the packing a cotyledon of the placenta

was adherent to the gauze. Two days following the condition of the patient was satisfactory but on the third day there was a rise of temperature and pulse with considerable secretion of milk. The breasts were so swollen that the movement of the arms was painful. The secretion of milk lasted nearly three weeks after the abortion. The patient stated that she had been delivered of a child five months before and that the midwife in attendance had delivered the placenta with the hand and that there had been no possibility of conception since that time. Evidently this retained portion of placenta which had been removed with the gauze was the cause for the free secretion of milk.

The writer also reports the case of a multipara pregnant for about six months, who expelled a fetus of about three months, mummified, with a placenta corresponding in size and development to five months. The placenta showed a subchoreal hematoma. The patient made a good recovery but two days after the expulsion of the dead fetus, the secretion of milk developed in abundance and proceeded for sometime. His third case was that of a multipara who believed herself pregnant seven months when the active movements of the fetus ceased. Two days later there was a secretion of milk, which persisted for six days. A seven months macerated fetus was expelled accompanied by the placenta and this showed areas of coagulation necrosis. These cases seem to indicate that the substances formed in the placenta and transmitted to the circulation furnishes a stimulus which excites mammary secretion. The writer states that the crisonogenous hormone which stimulates the secretion of milk is secreted by the myometrial glands. It is not thought that the fetus has any influence in determining mammary secretion. During pregnancy the internal secretion of the myometrial glands goes to the placenta, thence to the fetus, determining certain crises of development in the newborn to which Bar has called our attention. When the direct connection between the placenta and the uterus is interrupted the secretion of the myometrial glands passes into the blood of the mother and stimulates mammary secretion. Uterine involution is favored by the passage of the crisonogenous hormone into the maternal blood. These substances are found in greater or smaller quantity in the fetus, placenta and uterine tissue and this fact explains the results obtained by those who have used these substances in stimulating mammary secretion.

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## GYNECOLOGY

UNDER THE CHARGE OF

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**Radiotherapeusis in American Gynecology.**—The application of radiotherapy to various gynecologic conditions had become a well established practice in Europe before the outbreak of the war, the

leaders in this movement being several of the large university clinics of Germany. Taken up to a considerable, but somewhat less degree in France, radiotherapy was for some years looked at with much scepticism by the gynecologists at large in this country, and it is only comparatively recently that reports in any number have appeared in our literature concerning the gynecologic uses of the Roentgen-ray radium, and similar agents. The pioneer in this work in this country was Kelly, of Johns Hopkins; he is able to furnish statistics that both quantitatively and qualitatively compare favorably with those of any of the foreign clinics. In a recent resumé of some of his experiences with radium as a therapeutic agent in various malignant conditions, KELLY (*Am. Jour. Surg.*, 1916, xxx, 76) says that from January 1, 1909 to January 1, 1915 he has treated 213 cases of carcinoma of the cervix uteri. Of these, 10 were operated upon; 4 more might have been considered operable, but for various reasons were not operated upon; the remaining 199 were inoperable, either primarily, or were inoperable recurrences after operation. The 10 operated cases were subsequently subjected to prophylactic radiation, and all are apparently well at intervals ranging from six months to two years since operation. Of the remaining 203 cases, 57 are "clinically cured," 109 markedly improved and 37 not improved. In judging these results, it must be taken into consideration, however, that only 1 case of the entire series has passed the five-year limit, now pretty universally agreed upon as the minimum time in which we may speak of a "cure;" the others range from six months to four years since treatment. Kelly says that as a result of his experience in these cases, the following rules have been evolved as being the expression of his present policy: (1) Operate on every operable case, estimated as a good risk, as heretofore; (2) radiate for four to six weeks after operation; (3) do not operate on borderline cases, but use radium first, for the disease practically always returns after operation in these cases, while many are curable by radium; (4) radiate all advanced inoperable cases; for many of these too are curable, or can be shrunk down so as to become good risks; (5) where there are metastases up into the abdomen radiation may give great relief and a temporary return to apparent good health, but it will not cure. Kelly points out that it is very important to keep all these cases under occasional observation for some years, as a slight relapse is not infrequent, and as a rule responds readily to another application of radium. He feels that even if radium never actually cured a single case, it would nevertheless be an inestimable boon because of the prolonged relief which it gives from pain, with checking of offensive discharges, and general improvement in health and interest in life that it affords to sufferers from uterine cancer. Impressions obtained from a much smaller series of cases, observed over a shorter period of time, have been reported by MILLER (*Surg., Gynec. and Obst.*, 1916, xxii, 437) at a recent symposium of the Chicago Gynecological Society on Cancer of the Uterus. Since May, 1914, Miller has treated 26 cases of inoperable and recurrent cancer of the cervix with radium, and has followed the cases up to December, 1915. It is obvious, therefore, that absolutely nothing can be said as to ultimate results. Of 15 inoperable cases treated solely with radium, 4 have died and 2 are slowly succumbing; 5 are at present apparently free subjectively and

objectively of the disease; 4 showed evidence of returning trouble about six months after treatment, but have responded so far to further applications. In common with others, Miller has been astonished at the tremendous local benefits observed in practically all cases in the way of checking hemorrhage and discharge, and deodorization. In a number of cases excochleation and cauterization had been practiced a few months prior to the institution of radium treatment, but Miller does not approve of this procedure, since he is convinced that in these cases a longer time was required to check the local symptoms, and the subsequent histories do not show that they remained well any longer for having had the preliminary cauterization. In 6 cases radium was applied to malignant areas reappearing in the vaginal vault after hysterectomy—an extremely hopeless condition under ordinary circumstances. In four of these patients the growth promptly responded to the treatment, but as yet nothing can be said as to the ultimate outcome. In one case the mass soon disappeared, but the patient soon died from an infected kidney, and in the sixth, local masses have responded twice within the past year, but the patient is gradually going down hill. Miller emphasizes that his paper can be considered merely a preliminary report of experiences to date, but considers that while they in no way prove that radium can cure cancer, the results so far are superior to any other method that he has used in similar cases. His technic is to employ from 75 to 85 milligrams of radium element, endeavoring to give 3000 to 5000 milligram hours within a week or ten days, further applications being made a month later according to the indications. The question of gynecologic radiotherapy by means of the Roentgen-ray tube rather than radium has recently been discussed by LANGE (*Am. Jour. Roentgenol.*, 1916, iii, 72), who reports the results obtained in a series of 50 cases of benign conditions, such as menorrhagia, dysmenorrhea, and uterine myomata. He says that since the perfection of the Coolidge tube this form of treatment has been put on a much more satisfactory basis than formerly, since many of the technical difficulties of applying sufficient dosages have been removed. Whereas with the old equipment most roentgenologists who had interested themselves in gynecologic work had concluded that forty years was about the lowest age at which the artificial menopause could be produced with certainty, with the Coolidge tube there is no age limit beneath which it is not feasible to produce this result at will. In his series there were two patients of seventeen, and one of nineteen years, in whom an apparently permanent menopause was produced without difficulty. He therefore feels justified now in promising definitely that this result can be achieved in all cases in which malignancy, or inflammatory conditions such as pus tubes, can be excluded. In his series of 50 consecutive cases cessation of menstruation was secured in all in which it was desired, irrespective of age, and this as a rule exceedingly promptly. Lange says he has found it to be a safe working rule that when one period is missed all treatments may be stopped, since it is almost certain that though there may be an occasional showing subsequently, permanent cessation of menstruation will finally result. The dosage required to accomplish this varied in his cases from 100 X (one treatment) to 800 X (eight treatments). In 1 case a severe menorrhagia was reduced to a condition of normal menstruation, treatment

being stopped before complete amenorrhea was reached, and the author feels that with increasing mastery of the technic this ideal result may be looked for with much greater frequency in the future.

**Reno-renal Reflex Pain.**—The fact that unilateral renal pain, due apparently to a definite lesion in one kidney, but referred to the kidney region of the opposite side, may occasionally occur has long been known to the profession, but owing to the rarity of the phenomenon its possibility is often overlooked, thus leading to serious errors in diagnosis and treatment. An unusually striking and interesting example of this condition has recently been studied by FOWLER (*Surg., Gynec. and Obst.*, 1916, xxii, 454) and reported before the American Association of Genito-urinary surgeons. The patient was a young woman, aged twenty-nine years, who when first seen was suffering with what appeared to be a typical attack of renal colic, the pain being confined entirely to the right side. Ten years previously she had had an attack of hematuria, followed in a day or two by a very severe attack of kidney colic, the pain being localized in the right side. Five years later, after an interval of perfect health, she had a second similar attack, since which there had been no further pain up to the onset of the attack for which she came under Fowler's care. There had never been any pain on the left side, and no vesical irritation. Examination showed no tenderness, muscular rigidity, or pain to palpation of the left kidney region, but distinct pain, tenderness, and slight muscular rigidity on the right side. A Roentgen-ray examination showed a distinct shadow opposite the cartilage between the third and fourth lumbar vertebrae on the left side; the right kidney and ureter and left kidney were negative. A wax tipped catheter introduced into the left ureter met an obstruction at a point 24 cm. from the ureteral orifice, but by rotating could be passed by it into the kidney pelvis. Examination of the catheter on removal showed deep spiral grooves cut in the wax, evidently due to a stone in the ureter at a point 24 cm. from the bladder orifice, and just corresponding to that indicated by the Roentgen-ray. Catheterized specimens from each side showed a heavy ring of albumen and many leukocytes on the left, with no albumen and no leukocytes on the right. The output of urea was also greatly diminished on the left. In view of these findings, Fowler considered the diagnosis of stone in the left ureter justified, in spite of the fact that all symptoms had been on the right side. This diagnosis was confirmed at operation, an oblong, grayish-white stone having a surface bristling with sharp pointed crystals being removed from the left ureter. Convalescence was satisfactory, and there has been no recurrence of the pain in the right side up to the time of writing, eleven months after operation. The case above outlined is certainly of great interest, not so much from the standpoint of its curiosity, but from the emphasis that it throws upon the necessity of the most thorough examination by all the modern diagnostic means at our disposal of both kidneys and ureters in all cases of suspected renal or ureteral lesion. Had attention in this case been directed merely to the apparently affected side, the condition would not have been cleared up, and a serious but entirely useless operation might have been performed upon an entirely healthy kidney.

## OTOLOGY

UNDER THE CHARGE OF

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**Acoustic Injury and Personal Prevention of Occupational Deafness.**—Numerous writers, including SIEBENMANN (*Korrespond. f. Schweiz. Aerzt.*, 1915, No. 13), have given evidence, on the basis of experimental observation, that acoustic violence results in pathological changes in the labyrinth, the injury being primarily exhibited in the organ of Corti, later the efferent nerves and the proximate ganglia and finally in the body of the cochlear branch of the auditory nerve. The degenerative process in the nerves is to be regarded as secondary and progressive, and in reference to location, varies with the character and the path of intrusion of the acoustic shock. In reference to the question as to the direction of access of the sound waves to the labyrinth and the possibility of communication of acoustic shock through the medium of the body or the major access through the oval window, the author made elucidative investigations. By extraction of the incus, the sound transmission through the middle-ear mechanism was done away with, and in the animals thus treated, exposure to loud noise produced no intralabyrinthine injury, the conclusion being that aerial sound conduction through the sound-transmitting apparatus of the middle ear was the major path of transmission and that, for personal protection from occipital noise, the stoppage of the external auditory canal is of primary importance, the isolation of the body of the workman, by means of felt soles and rubber gloves, being unnecessary.

**Aural Implication in Diabetes Mellitus with Especial Reference to the Internal Ear.**—In all of the cases in which protracted observation was possible there was evidence of a slowly progressive depreciation in the hearing power, the result of the cumulative degenerative change in the cochlear nerve and the cell elements of the organ of Corti. The symptoms of most prominence, according to the observations of EDGAR (*Monatschr. f. Ohrenh.*, 1915, xlix), in addition to the impairment of hearing, were the occurrence of subjective sounds and attacks of vertigo; in the great majority of the cases both ears were similarly affected, so far as impairment of hearing was concerned. In but 1 out of the 52 cases recorded was the impairment of hearing of sudden onset, in all the others the beginning of the impairment and its progress had been unappreciated, indeed the majority of the patients made no unsolicited reference to the hearing which was found to be impaired only upon examination and test. This observation may, in the opinion of the author, be in part accounted for by the recognized fact that, in long-standing cases of diabetes, there is a general weakening of the reflex functions including a certain acoustic dulness so that a creeping progressive deterioration of the hearing power would not be appreciated. In very nearly one-half of the cases subjective sounds

were reported in one or in both ears, more frequently intermittent, but in some cases continuous. In 3 cases, for six months under observation, the subjective sounds at first reported ultimately disappeared. In 6 of the cases there was labyrinthine vertigo. In 3 of these the attacks were of short duration only and apparently the sequence of some psychic excitation or muscular exertion. In 1 case only were the attacks fulminant. Spontaneous nystagmus was demonstrated in only 1 or 2 cases and then in moderate degree. In about one-quarter of the cases there were disturbances of equilibration in a very moderate degree and there were only 3 cases in which the patients could not maintain the Romberg position or balance upon one foot. The diagnosis of the aural implication in diabetes presents no difficulties. The history in any given case, together with the results of the acoustic tests, a positive Rinné, lessened hearing by bone conduction, a nearly normal hearing for tones of medium low pitch, lessened hearing for tones of high pitch, aurally conveyed, without corresponding objectively observable cause in the middle-ear sound-transmitting apparatus, coupled with a general physical examination, eliminative of other general causes for the labyrinth affection, are distinctly determinative of the true condition. As concerns the course and the prognosis of this peripheral concomitant of diabetes, it is especially chronic in its development and continuity; the patients are rarely able to indicate, even approximately, the time of the beginning of the aural symptoms; a moderate degree of impairment of hearing passing unnoted and its gradual progress, without acute variations, presenting nothing especially worthy of remark. In 1 case of a high grade of deafness, ten weeks' observation showed no change. In 3 cases of moderate impairment of hearing and 1 case of a medium grade of impairment, an examination, when repeated at the end of two months, showed a slight gain in the general hearing power, which gain was subsequently lost, the improvement being coincident with persistence in a strict antidiabetic diet and the urine being free from sugar. In reference to treatment it was uniformly observable that there was an improvement in the hearing so soon as the urine was free, or nearly free, from sugar and that depreciation in hearing was found to be coincident with any subsequent increase in the sugar percentage in the renal excretion. Local aural treatment is of no avail in these cases. Galvanization of the acoustic nerve has been suggested and applied without, however, any demonstrably good effect; the labyrinth affection in diabetes being intimately dependent for its course and progress upon the causative disorder. The fact that the impairment of hearing in cases of diabetes is so moderately in evidence in its beginning and the very positive dependence of the intralabyrinthine evidences upon the causative renal condition make the observations of the author and his following conclusions of especial value to the general practitioner since, in the paucity of aural manifestations there would be a comparatively lessened liability of reference to special investigation. The frequency of disease of the internal ear in diabetes and the fact, established in many cases, of an improvement in the hearing coincidently with the entire or comparative freedom of the urine from sugar and, contrariwise, a depreciation in hearing together with an increase in sugar percentage in the urine may be taken as indubitable evidence of the etiological relationship of the two phenomena. In a por-



tion of the cases there was a degenerative change in the internal ear implicating the auditory nerve the result of a toxic neurolabyrinthitis, while in still other cases the pathological changes in the labyrinth were the consequence of the arteriosclerotic changes in the bloodvessels, to which diabetics are especially prone.

**Experimental Investigations into the Traumatic Pressure Effect of Explosions.**—Recent experience in military operations shows that serious injury may be effected by windage or air compression incident to the immediate vicinity of shells in flight, even to the extent of fracture of the vertebrae in a man sitting in a bowed position, of which the scalping or denudation effect is a further example. F. RUSCA (*Deutsch. Ztschr. f. Chir.*, cxxxii, p. 315) endeavored to explain these effects in parallel by studying the influence exerted by gas and water compression upon rabbits and fishes, it being found that the influence exerted, through these media, in addition to the frequently recognizable rupture of the drum-head, resulted in serious injuries to the skull and to the brain, and to the latter when the cranium remained intact, as exhibited frequently during the present war in the form of hemorrhages at the base and at the convexity of the brain. The variety of injuries produced, including the ruptures of, and ecchymoses in, the membranous labyrinth is explained by the author by the radiated as well as by the direct pressure effect.

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## HYGIENE AND PUBLIC HEALTH

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**The Prevalence of Trachoma in Kentucky.**—In 1912 a survey made by the U. S. Public Health Service of seven counties in the mountain region of Kentucky, showed that 12.5 per cent. of the population of the counties examined were suffering from trachoma. This survey has been continued and the results of the later work have been published (*Public Health Reports*, March 5, 1915). It was found in the survey of twenty-three counties, 18,016 persons being examined, that 1280 cases or over 7 per cent. of those examined were suffering from trachoma. In some counties the percentage of persons found infected was as high as 26.4 per cent. while in others it fell to about 3 per cent. The majority of those examined were school children and the findings may be taken as representing fairly accurate conditions among adults. Almost all those examined were whites, as the negro population is very small in

the mountain section of Kentucky. Inasmuch as the bulk of the population in these counties comes from old American stock, foreign immigration cannot be blamed for the prevalence of the disease. The U. S. Public Health Service regards its estimate of 33,000 cases in thirty-five mountain counties as conservative, though approximate; and has established hospitals at various points for the treatment of the disease and the education of the general public as to the means of its prevention. Trachoma undoubtedly exists in many other places in this country. It is certainly widespread among the Indian tribes and the Public Health Service is endeavoring to eradicate the disease and prevent its spread.

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**The Experience of the New York City Health Department with Typhoid Immunization.**—HARRIS and OGAN (*Department of Health of the City of New York Reprint No. 22, January, 1915*) draw the following conclusions: (1) The accurate observations recorded in hundreds of thousands of cases leave no doubt as to the preventive powers of antityphoid vaccination in all but a relatively insignificant number; (2) In those subsequently affected it strikingly decreases severity of the disease and the mortality; (3) Severe reactions, if one makes observations from extensive studies (the only correct way) are rare; (4) To avoid severe reactions one must observe carefully several precautions, as follows: (*a*) Never administer it to any but the healthy; (*b*) To permit of slow absorption, avoid puncture of a vein, or intramuscular injection; (*c*) Clean syringe and sterilize the area for injection, using tincture of iodine for the latter purpose; (*d*) Children, especially, are to avoid exposure to the sun following treatment; (*e*) Avoid administering it during the menses or pregnancy; (*f*) Allow no hard work or indulgence in alcohol immediately after the injection; (*g*) Avoid reinjecting in indurated areas; (5) Severe reactions have never left permanent injury; (6) When the incubation period has begun, the time for antityphoid immunization has passed. The vaccine is a preventive of typhoid fever, and not a typhoid antitoxin; (7) Long exposure to overwhelming doses of typhoid bacilli as in those who are in close contact with cases and especially in epidemics, may nullify the immunization powers of antityphoid vaccine, and an attack may therefore incidentally follow one or more injection; (8) Chronic illness (tuberculosis, etc.), as well as debility from other causes, and fatigue and exhaustion also predispose to severe reactions; (9) Injection after intimate and long exposure hasten the onset; (10) For a period of at least two years, and possibly longer, immunization is as effective in protecting from an attack of typhoid fever as is a previous attack of the disease itself; (11) Infections may follow after a complete immunizing course of treatment, in exceptional instances in which debility and fatigue exhaust the resistant and defensive powers of the body, and when exposure to massive doses of typhoid bacilli exists.

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**A Survey of the Public Health Administration of the State of Washington.** The United States Public Health Service, has, in the last twelve months, been making a survey of certain State health organizations with a view of standardizing the operations of the various sanitary studies in the United States. It is hoped that the accomplish-

ment of this end will do much to bring about uniformity of action on the part of public officials and to further increase the efficiency of the various State and municipal health organizations. The results of the survey of the health administration of Washington have been published (*Public Health Reports*, February 5, 1915). The conclusion was reached that the adoption and enforcement of measures for the protection of the public health in that State have not kept pace with the economic growth of the State. An analysis is made of the various functions and activities of the Washington State Board of Health and certain recommendations are made, the adoption of which it is believed would meet the present public health requirements of that State. Briefly summarized, these recommendations are: That all public health activities now performed by the State should be brought together in a single department of health, to be subdivided into bureaus, with a commissioner of health as the administrative head and the State Board of Health as an advisory and quasilegislative body. The functions of the various bureaus are carefully outlined, and it is recommended that the State be divided into not less than fifteen health districts, each to be under a whole-time health officer of adequate training and experience in the science of public health. It is also recommended that the State be divided into three districts, each to be put under the supervision of a sanitary engineer. Provision is made for laboratories and the passage of various model laws, one for morbidity reports receiving especial attention. Up to this time the Public Health Service has made and published the results of surveys of health administration of the States of Minnesota, Maryland, West Virginia and Washington, and of the city of Baltimore. It has been announced that the service is now making health surveys of other States and of several cities.

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#### **The Milk Supply as a Causal Factor in Relation to Tuberculosis.—**

SHERIDAN DELÉPINE (*Journal State Medicine, Reprint*, November and December, 1914) states that it is impossible to measure accurately the amount of tuberculosis that is attributable to cows' milk because the various methods of investigation give widely different indications. There is, however, on many points, general agreement between observers; the differences relate chiefly to quantitative estimates. The information supplied by the various methods indicates: (1) That an exceedingly small number of children are tuberculous at birth; (2) That soon after birth they begin to contract the disease; (3) That the nature of the tuberculous lesions and their distribution show that before the fifteenth year the alimentary passages are important channels of infection, and that after the fifteenth year infection generally takes place through the air passages; (4) That, when the matter has been investigated, it has been found that among children suffering from tuberculosis other than pulmonary tuberculosis a great number have been fed on unsterilized cows' milk; (5) That from the lesions of children fed on unsterilized cows' milk, bacilli resembling those associated with bovine lesions are found in the great majority of cases; (6) That both the distribution of the lesions and the characters of the bacilli seem to indicate that not less than 20 to 25 per cent. of the cases of infantile tuberculosis are attributable to infection through cows' milk, and that

some results indicate a much higher proportion; (7) That experimental evidence shows that the ingestion of tuberculous cows' milk is followed by infection through the alimentary canal in the great majority of mammals on which the experiment has been made. Delépine concludes that it appears reasonable to say that, although there is not complete agreement in the results obtained by various observers as to the exact amount of human tuberculosis attributable to the consumption of tuberculous cows' milk, there is *clear and cumulative evidence that cows' milk plays a very important part in the production of infantile tuberculosis in England and Scotland.*

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**The Action of Anti-pneumococci Serum.**—C. G. BULL (*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 149) studied the cause of the disappearance of pneumococci from the blood, following an intravenous injection of a small amount of immune serum. He found that the immune serum actively agglutinated the pneumococci in dilutions of 1 to 500, when observed under the microscope, whereas macroscopically the agglutination titre is 1 to 80. Therefore, it was surmised that the disappearance of the bacteria from the circulating blood, following the injection of immune serum, might be due to clumping *in vivo*. Next, fragments of the organs—lungs, spleen, liver, kidney, brain, etc., were crushed and examined and clumps of pneumococci were found in all. The fate of the clumps was then investigated. By killing the rabbits at various times, after the administration of the serum, it was observed that the polymorphonuclear leukocytes englobed and digested them. The fixed cells play a small part also. Sectioned and crushed tissues gave the same results. Pneumococci from 150 c.c. of bouillon are thus destroyed within two to three hours. The smallest amount of serum that will influence the infection causes the clumping *in vivo*.

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**Chronic Lead Poisoning: Breeding Experiments.**—C. V. WELLER (*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 157) notes that there have been frequent clinical observations of the apparent deleterious effect upon the germ plasm exerted by chronic poisoning. A majority of these cases have been found in female lead workers and in these it might be supposed that abortions, stillbirths, and early deaths of infants were due as much to the toxic effect of lead during extra-uterine development as to an actual injury to the germ plasm. In the smaller number of instances in which the male parent alone was poisoned, the resulting sterility without impotency, the stillbirths and the early deaths of offspring are difficult to explain unless they are due to blastophthoria. The work of Stockard and of Cole and Davis has shown that alcohol has a similar effect. In a recent report which appeared as the present series of experiments was being concluded Cole and Bachhuber have demonstrated that the offspring of male rabbits poisoned by lead as well as of male fowls similarly poisoned are of distinctly lower vitality than the offspring of normal males. In attempting to determine experimentally whether blastophthoria occurs in chronic lead poisoning, guinea-pigs were given repeated weighed doses of commercial white lead in capsules by mouth. These guinea-pigs were mated, lead females with normal males and lead males with normal females. In order to check the results as efficiently as possible control matings were

made of normal males with normal females under the same feeding and housing conditions as the lead poisoned pigs, and for the same reason the normal females were bred alternately to lead males and to normal males. The dosage of lead was controlled by frequent weighings in order that the general nutrition should not be seriously impaired. A total of 93 matings yielded 170 offspring. Of these, 32 matings of normal male with normal female produced 58 offspring, with an average birthweight of 81.5 gm. From 34 matings of lead male with normal female 65 young were produced with an average birthweight of 69.3 gm. Nine offspring of lead males died in the first week against 2 offspring of normal males dying in that time. Eight young of lead females were stillborn against 3 stillborn from normal females bred to normal males. From the entire series of matings the following conclusions seem to be justified: (1) In chronic lead poisoning in guinea-pigs there is a definite blastophthoric effect which can best be demonstrated upon the male germ plasma. This effect manifests itself in some instances by sterility without loss of sexual activity, by a reduction of 20 per cent. in the average birthweight, by an increased number of deaths in the first week of life and by a retardation in development such that these pigs remain permanently underweight. (2) From the apparent recovery of the germ plasma some time after stopping the administration of lead it seems that the deleterious effect must be suffered especially by that portion of the germ plasma which is undergoing maturation and not by that which is stored in the primary germinal epithelium. However, final judgment upon this point must be withheld.

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## PATHOLOGY AND BACTERIOLOGY

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**The Effect of Antibody Production of the Removal of Various Organs.**  
—HEKTOEN and CURTIS (*Jour. of Infect. Dis.*, 1915, xvii, 409) carried on a rather remarkable series of experiments to determine the part played by certain organs in the production of antibodies. The experiments were performed on dogs immunized against rat blood, and the agglutinins and opsonins were determined. The control animals showed maximum antibody production on about the twelfth day followed by a gradual defervescence to the normal level on about the fortieth day.

Other animals, following an immunizing inoculation were subjected to various operations in which some abdominal or other viscus was removed. It was found that complete removal of the stomach, of the small intestine or of the thyroid did not interfere with the development of the antibodies studied. Removal of the pancreas, complicated by intussusception and rabies, showed lessened production of the immune substance. Simultaneous removal of the spleen and pancreas also inhibited antibody production simulating the removal of spleen alone. Removal of the small intestine and ligation of the mesenteric artery increased the latent period preceding the appearance of the antibodies. Adrenalectomy did not influence the antibody curve. The authors conclude that the production of antibodies is not influenced by certain disturbances and that their results in no way contradict the view that these mechanisms are located in the blood-forming organs.

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**Clinical and Experimental Observations upon the Pathology of Trench Frost-bite.**—The work upon this subject was stimulated through the numerous cases of frost-bite occurring among the invalided soldiers on the continent. SMITH, RITCHIE and DAWSON (*Jour. Path. and Bacteriol.*, 1915, xx, 159) point out that this has been not uncommon in previous military campaigns, the most notable of which was Napoleon's Russian Invasion. The trench frost-bite has to do entirely with the feet, the exposed hands and face escaping. This is the result of the fact that the feet are tightly enclosed and exposed to semi-frozen mud. Experiments on frost-bite were also undertaken on animals. The essential change in the frost-bite consists in damage of the bloodvessels. After an initial constriction, the exposed vessels show cellular change in their walls which alters their function and permits an excessive amount of fluid to be poured into the surrounding tissue when the cold is removed. The injury is also accompanied by the infiltration of inflammatory cells. The involved areas also suffer the lack of nutrition from vascular constriction with sluggishness of the circulation. The lymphatics of the part are much dilated so that their function is impeded and the tissue fluids are stagnant. Diffuse hemorrhages are also commonly found. They observed that these experimental lesions were very similar to the spontaneous processes in man.

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**Cardiac Lesions in Goitre.**—Disturbance of heart are not alone found in exophthalmic goitre, but also in those of the colloid types. In the latter, it is claimed that the heart suffers mainly from mechanical disturbances of the circulation, rather than as a result of intoxication. To all forms of these cardiac disturbances the term "Kropfherz" is given. There have been relatively few pathological examinations of the heart in goitre, although much data is at hand of clinical studies. Schantz has reported the macroscopic appearance of the heart tissues in cases of colloid goitre, but he has failed to study the tissues histologically. A fatty degeneration of the tissue has been described by several. Bircher studied the hearts of rats in which an experimental goitre had been induced by giving them water from a goitrous district.

The heart muscle, he believes, is directly injured by the harmful agent in the water, this agent, he thinks, attacks the heart and thyroid simultaneously. The majority of authors believe that the injury to the heart is due to a toxic substance liberated by the thyroid. Simmonds examined 8 cases of Basedow, in 7 of which a slight fatty change was found. The histological findings are insufficient to explain the marked clinical symptoms. FAHR (*Centralbl. f. Pathol.*, 1916, xxvii, 1) studied 8 cases of goitre heart, 5 of which were of the Basedow type and 2 of colloid goitre. Two cases of Basedow occurred in girls of twenty-one years. The heart of one was hypertrophied and of the other reduced in size, the muscle tissue of each showed an acute interstitial myocarditis with leukocytic infiltration. The heart muscle showed evidence of degeneration. In two older individuals there was a similar but milder infiltration with fibrosis. Histological changes were found in the muscle tissue of all cases. There was no evidence that the vascular structures of the heart were primarily involved. The author believes that the toxin associated with goitre has a direct effect upon the heart muscle.

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**Thrombosis of the Mesenteric Arteries.**—INGEBRIGSTEN (*Centralbl. f. Path.*, 1915, xxvi, 313) reports 2 cases of thrombosis of the superior mesenteric artery, illustrating the marked difference from embolism of the same vessels. Both of these were observed at autopsy. The thrombosis had developed within leucic vessels. In neither case was there evidence of infarct nor had there been any abdominal symptoms during life. He also reported a third case developing in a patient with mitral endocarditis in which multiple small emboli were followed by thrombosis and infarction of the intestine. Curiously enough, both anemic and hemorrhagic infarcts were present in the bowel.

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**The Effect of Antiplatelet Serum on Blood Platelets and the Experimental Production of Purpura Hemorrhagica.**—For some years attention has been directed to the part played by blood platelets in purpura hemorrhagica. Although none of the studies claim that the abnormal condition of the platelets is the prime factor in this blood dyscrasia, yet it would appear that the influence of various toxic and bacterial agents leads to a sufficient disturbance of these elements that hemorrhagic processes are a common outcome. The work of Duke, Cole and Ledingham has indicated the importance of platelet disturbance under these conditions. LEE and ROBERTSON (*Jour. Med. Research*, 1916, xxxiii, 323) obtained an antiplatelet serum by repeatedly injecting a rabbit with guinea-pig platelets. This rabbit serum had both lytic and agglutinative properties which were specific for guinea-pig platelets. They found that the phenomenon of lysis required the presence of complement. In another series of experiments, they found by the inoculation of the antiplatelets serum subcutaneously, intraperitoneally, or intracardiac into guinea-pigs, gave rise to purpura in various grades of intensity. By the intracardiac method, death was produced with relatively small amounts of serum. Hemorrhages occurred in various parts of the body including the intestines. Sometimes the bleeding began within a few hours after the injection. The

platelets in all instances were markedly reduced, falling as low as 16,000. The clotting time of the blood was not altered, although the blood clot showed no contraction on standing. The histological examination of the hemorrhagic areas gave no information as to the manner in which the hemorrhages were produced.

**Diabetes Insipidus.**—Among the many theories in explanation of diabetes insipidus, attention has been particularly attracted to the nervous system and the glands of internal secretion. The apparent association of cerebral injuries, tumors of the brain, and chronic meningitis with diabetes insipidus has been repeatedly commented upon. More and more, however, the cerebral disturbance has been localized about the hypophysis. Hewlitt, Frank, Simmonds and others were the first to observe the presence of polyuria with disturbances of the pituitary body. Some claimed that the disturbance was due to an oversecretion by the pars intermedia, while others believed that the result was obtained by a diminished function on the part of the pars intermedia, while others believed that the result was obtained by a diminished function on the part of the pars intermedia and the posterior lobe. MEYENBURG (*Ziegler's Beiträge*, 1916, lxi, 550) reported two further cases of diabetes insipidus in which the pituitary body was diseased. The first case was a woman, aged thirty-six years, suffering from symptoms of brain tumor associated with polyuria. At autopsy a tuberculous process was found at the optic chiasm and hypophysis. The posterior lobe was particularly involved. The second case also had manifestations of a cerebral tumor with polyuria and polydipsia. At autopsy a malignant tumor was found surrounding the pituitary. In both cases histological examination showed an almost complete destruction of the middle and posterior part of the hypophyseal gland. The author carried on a series of experiments in which animals were treated by repeated injections of pituitary extract. He was unable to obtain any conclusive results respecting the quantity of urine secreted. The author points out that as many of the endocrinous glands are composed of two or more functionally active tissues it is impossible to separate the pathological process of one from those in the other. It is probable that there is a close interdependence between these tissues of the ductless glands so that the activity of each is closely related to the healthy function of the other. Such interactivity is claimed for the components of the adrenal gland. He then concludes that diabetes insipidus of pituitary origin is not due to a hyper- or hypofunction of the one or other portion of the hypophysis but that a disturbance of any portion is reflected to all portions of this gland. Thus a pathological process situated in any part may disturb the function of the entire hypophysis with diabetes insipidus as one of the manifestations.

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